Examining Cognitive Fatigue in Multiple Sclerosis: Can Self-Reported Fatigue Predict Deteriorating Test Performance?

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Statement of Sources

I declare that this report is my own original work and that the contributions of others have been duly acknowledged

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Caitlin Turner Date

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List of Acronyms

CNS	Central Nervous System
FIS	Fatigue Impact Scale
FSS	Fatigue Severity Scale
HC	Healthy Control participants
HRT	Hit Response Time
MFIS	Modified Fatigue Impact Scale
MS	Multiple Sclerosis
PPMS	Primary-Progressive Multiple Sclerosis
pwMS	People with Multiple Sclerosis
RRMS	Relapse-Remitting Multiple Sclerosis
SPMS	Secondary-Progressing Multiple Sclerosis
VAS	Visual Analogue Scale
VAS-F	Visual Analogue Scale to Evaluate Fatigue Severity

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Abstract

Multiple Sclerosis (MS) is the most prevalent neurological disorder affecting younger adults. A symptom affecting the majority of people with MS (pwMS), and which can significantly impede the person's ability to engage in everyday activities, is fatigue. This study aimed to further current understandings of the little understood concept of cognitive fatigue in pwMS. Cognitive fatigue was examined through *objective* and *subjective* (intellectual and online) measures. Participants included 31 pwMS (M = 47.77, SD = 12.19) and 30 healthy controls (M = 44.37, SD = 11.37), who completed neuropsychological assessments, including a task of sustained attention administered twice during testing. Participants completed a single intellectual assessment of cognitive fatigue, and online assessments of cognitive fatigue repeated three times throughout testing. The findings indicated that fatigue in MS is experienced temporally, with higher self-reports of fatigue following sustained mental effort. The online measures were the strongest predictor of actual test performance. Further, pwMS overestimated their levels of fatigue relative to actual test performance indicating possible reduced levels of insight into actual declining abilities. The results highlight the need for clinicians to utilise various measures when examining the multifaceted phenomenon of cognitive fatigue, and address perceptions pwMS may have about their fatigue.

Examining Cognitive Fatigue in Multiple Sclerosis: Can Self-Reported Fatigue Predict Deteriorating Test Performance?

Multiple sclerosis (MS) is the most prevalent neurological disorder affecting younger adults in the developed world (Palmer, 2011). Whilst the symptoms and progression of MS are highly heterogeneous, arguably its most pervasive and debilitating symptom, experienced in up to 87% of people with MS (pwMS), is fatigue (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989). Fatigue is defined as a *subjective* lack of physical and/or mental energy that interferes with usual or desired activities, social behaviour and psychological wellbeing (DeLuca, 2005). Importantly, fatigue can considerably impact everyday functioning, even in the early stages of the disease (Benedict et al., 2002; Simmons, Tribe, & McDonald, 2010). However, despite its significance, the experience of *cognitive fatigue* still remains poorly understood and defined (Genova et al., 2013). Developing an increased understanding of the nature of cognitive fatigue in MS is vital, not only to improve the assessment and diagnostic proficiencies of clinicians working with MS patients, but also for the provision of more effective remediation and compensation strategies which aim to improve the quality of life.

MS Characteristics

MS is a chronic progressive autoimmune disease of the central nervous system (CNS), characterised by inflammatory demyelination of both grey and white matter (Genova et al., 2013; Harbo, Gold, & Tintoré, 2013; Trapp & Nave, 2008). Demyelination occurs as a result of the destruction of myelin sheaths and oligodendrocytes (myelin-producing cells), which causes scar-like lesions. These lesions, sclerotic plaques, can distort or block transmission of neural impulses (Bitsch, Schuchardt, Bunkowski, Kuhlmann, & Brück, 2000; Bjartmar & Trapp,

2003; Trapp et al., 1998). The accumulation of sclerotic plaques, and eventual axonal and neuronal degeneration, can lead to permanent impairment of movement, sensations, and cognition (Bjartmar & Trapp, 2001). Lesions can occur in any location throughout the CNS, commonly affected areas include the spinal cord, subcortical white matter and the cortex (Brassington & Marsh, 1998). As a result of varying anatomical locations that can be impacted, the symptoms and trajectory of the disease also vary, making MS highly heterogeneous (Brassington & Marsh, 1998; Lee, Taghian, & Petratos, 2014).

The most common types of MS are: relapsing-remitting (RRMS), secondary-progressive (SPMS) and primary-progressive (PPMS; Lublin & Reingold, 1996; see Figure 1). Other classifications include: progressive-relapsing (PRMS), benign and cortical MS. RRMS affects 80 percent of pwMS and is typically seen in the initial stages (Noseworthy, Lucchinetti, Rodriguez, & Weinshenker, 2000). The average age of RRMS diagnosis is 30 years, and it is three times more prevalent in females (Miller & Leary, 2007). RRMS is characterised by periods of disease relapse, significant worsening of neurological symptoms over several days, followed by disease remission (symptomatic improvement). Relapses are assumed to be a direct result of active inflammatory lesions, and accompanying myelin loss, which slows or blocks neural transmissions (Centonze et al., 2010). A relapse is defined as the occurrence, recurrence or worsening of symptoms that lasts over 48-hours. These symptoms must not be associated with fever, and occur at least 30-days after improvement/stability (Schumacher et al., 1965). Remission occur as a result of inflammation resolution, where the sodium (Na+) channels along demyelinated axons, and re-myelination of affected nerves, are reorganised (see Figure 2; Trapp & Nave, 2008). Remission occurs spontaneously, or in response to corticosteroid

medication.

Following a period of 10 to 15 years, approximately half of individuals with RRMS develop SPMS (Trapp et al., 1998). Relapses are less apparent due to continually worsening symptoms. Periods of spontaneous remission are no longer experienced and corticosteroid medications become ineffective, resulting in eventual axonal destruction (see Figure 3). This is the result of amyloid precursor protein accumulation in the nerve, resulting in permanent deficits (Trapp, Ransohoff, Fisher, & Rudick, 1999).

PPMS, a common sub-type of MS, affects approximately 15 percent of pwMS. Unlike RRMS, prevalence of PPMS is equal amongst both sexes, and age of diagnosis is approximately 40 (Miller & Leary, 2007). PPMS is characterised by continual worsening of symptoms without defined relapses or remissions (Lublin & Reingold, 1996; Miller & Leary, 2007).

As previously mentioned, the symptoms of MS are highly variable and thought to be dependent on the locations where lesions develop (Goverover, Genova, Griswold, Chiaravalloti, & DeLuca, 2014). Traditionally MS has been viewed as a disease where the neurological deficits result exclusively in physical impairments. Symptoms commonly experienced by pwMS includes weakness, tremors, tingling, numbness, paralysis, vertigo, pain, and physical fatigue all resulting in reduced mobility. PwMS may also suffer from bladder and bowel disturbances, vision and other sensory impairments, and sexual dysfunction (Thompson, 2001).

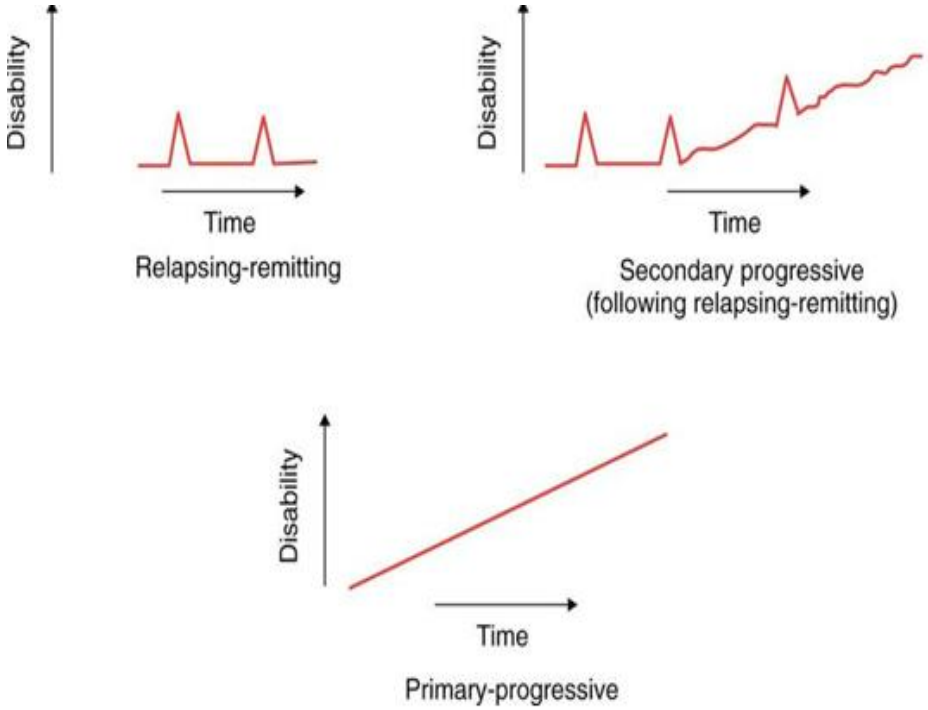

Figure 1. Clinical courses of MS. Adapted from "Defining the clinical course of multiple sclerosis: results of an international survey. National Multiple Sclerosis Society (USA) Advisory Committee on Clinical Trials of New Agents in Multiple Sclerosis" by F. D., Lublin, and S. C. Reingold, 1996, *Neurology, 46,* p. 909.

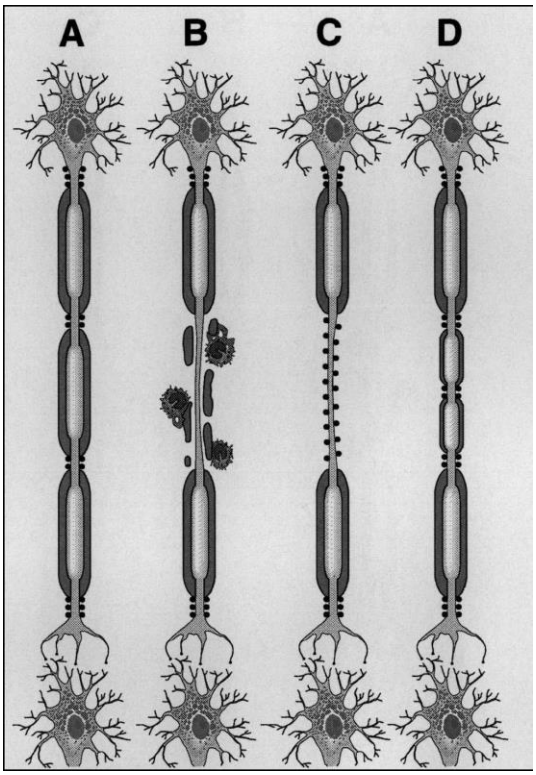

Figure 2. The pathogenic process of demyelination and remyelination in MS. (A) Normal myelinated fibers; (B) demyelination by inflammatory processes which causes conduction blockages; (C) Na+ channel redistribution; (D) re-myelination. Both C & D restores and contributes to clinical remission. From "Neurodegeneration in Multiple Sclerosis: Relationship to Neurological Disability", by B. D. Trapp, R. M. Ransohoff, E. Fisher, and R. A. Rudick, 1999, *Neuroscientist, 5,* 49.

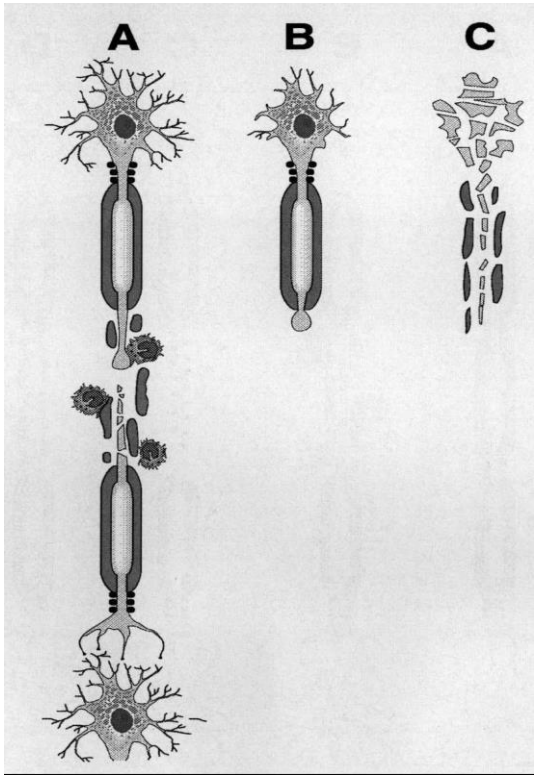

Figure 3. Axonal transection during inflammatory demyelination. (A) Axonal transection which is a consistent feature of inflammatory demyelination lesions. This results in (B) degeneration of the distal axonal segment and (C) irreversible loss of neuronal function. From "Neurodegeneration in Multiple Sclerosis: Relationship to Neurological Disability", by B. D. Trapp, R. M. Ransohoff, E. Fisher, and R. A. Rudick, 1999, *Neuroscientist, 5,* 50.

Over the previous two decades, there has been increasing research highlighting that in addition to physical symptoms, cognitive impairments are also highly prevalent in pwMS (Goverover et al., 2014). Cognitive impairments have been found to affect individuals at any stage throughout the disease and can occur independently from physical impairments (Benedict et al., 2002). It is reported that cognitive difficulties affect up to 65 percent of pwMS, which in turn can negatively affect quality of life through reduced social interactions, difficulty performing

household chores and withdrawal from work (Honan, Brown, & Batchelor, 2015; Rao, Leo, Bernardin, & Unverzagt, 1991). Benedict et al. (2006), interested in the domains affected in pwMS, developed and validated the Minimal Assessment of Cognitive Function in MS. Through a principle components analysis, they revealed three general domains of impairment: processing speed/working memory, memory, and executive function. These findings were supported by Chiaravalloti and DeLuca (2008).

Cognitive fatigue

Cognitive fatigue, whilst largely viewed as a subjective experience, can be examined through objective and subjective measures (see Figure 4). Objectively, cognitive fatigue is believed to be examinable through deficits on standard neurological tests (Krupp & Elkins, 2000). However, the explanation as to why impairments occur as a result of fatigue is still under debate (Sandry, Genova, Dobryakova, DeLuca, & Wylie, 2014). One proposed explanation is that impairments are secondary to fatigue (Coyne et al., 2015). This is not to say all cognitive impairments are due to fatigue, but rather, it is likely that performance becomes undermined by fatigue. The effect of fatigue on performance has been examined in relation to physical symptoms, where it was found that 6-minutes of walking resulted in increased subjective reports of physical fatigue, as well as objective increases in postural sway and reduced lower limb strength in pwMS (McLoughlin, Barr, Crotty, Sturnieks, & Lord, 2014). These findings suggest that sustained physical effort results in impairments. However, the effect that sustained mental effort has on *cognitive abilities* remains poorly understood (Sandry et al., 2014). This is despite research indicating that pwMS link their cognitive dysfunction to cognitive fatigue; known clinically as the “fatigue cascade effect” (Coyne et al.,

2015). The inadequate examination of the relationship between the experience of cognitive *fatigue* and *impairments* may be due to the lack of consensus on methods for examining both subjective and objective cognitive fatigue (DeLuca, 2005).

Cognitive fatigue is typically assessed through self-report, both clinically and in prior research. Branas, Jordan, Fry-Smith, Burls, and Hyde (2000) report that there are two 'types' of fatigue that pwMS experience. There is the experience of an abnormal, constant and persistent sense of tiredness, as well as the experience of increased tiredness in direct response to undertaking specific tasks, or as the day progresses. These experiences have recently been, coined by Genova et al. (2013) as *trait fatigue* and *state fatigue*. Whereas trait fatigue is assessed using 'intellectual' self-report measures (i.e., over an extended period of time), state fatigue is assessed using 'online' self-report measures (i.e., the current point in time). The majority of research has focused on the experience of trait fatigue, with research into state fatigue being limited (Krupp & Elkins, 2000; Sandry et al., 2014).

To date, research has failed to find a relationship between objectively measured (neurological testing) and subjectively reported cognitive fatigue (Paul, Beatty, Schneider, Blanco, & Hames, 1998). However, this may be due to the techniques used to assess both objective and subjective cognitive fatigue. Thus, the current paper more specifically attempts to clarify the relationship between subjective (*trait* and *state*) and objectively measured fatigue.

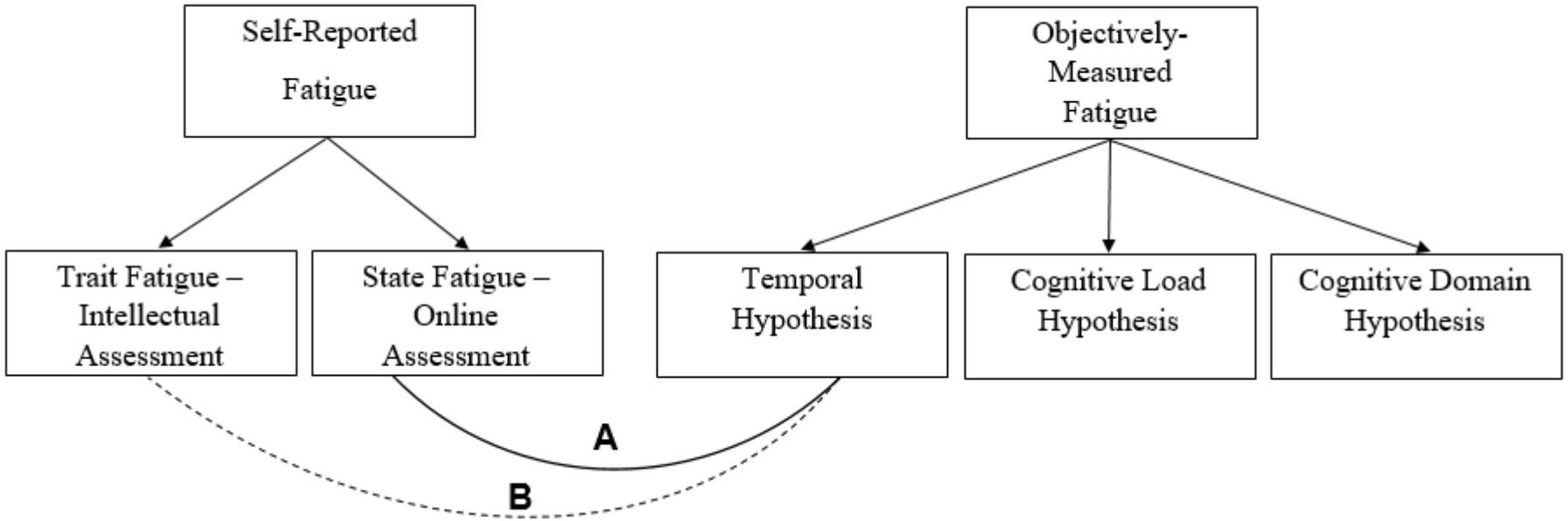

Figure 4. Schematic overview of the methods available for assessing cognitive fatigue. The current study is assessing (A) Online awareness is the association between a subjective measure fatigue, an online assessment of (state fatigue) and the objective measure of declining performance over time (temporal hypothesis). The current study also examines (B) Intellectual awareness is the association between intellectual assessments of fatigue (trait fatigue) and declining performance over time.

Subjective Measurement of Fatigue

The ability to assess subjective measures of fatigue, whether cognitive or physical, is largely dependent on individual's *awareness* into their cognitive or physical state. Self-awareness has traditionally been defined through a hierarchical pyramid model, with progression to higher levels dependant on successful attainment of preceding levels (Crosson et al., 1989). At the base of the pyramid is *intellectual awareness,* which refers to the general ability to show understanding of difficulties experienced. Individuals who possess advanced intellectual awareness have the ability to recognise the ramifications of their impairments. The second level is *emergent awareness.* This refers to the ability to recognise impairments as they occur and consequently engage in compensatory strategies. The most advanced level of self-awareness is *anticipatory awareness*, which refers to the ability, not only to be aware of impairment, but also to anticipate when problems will arise.

In contrast, Toglia and Kirk (2000) postulate that self-awareness is a dynamic process, consisting of metacognitive knowledge and online awareness. They argue that metacognitive knowledge (also referred to as 'intellectual' awareness) refers to an individual's knowledge of task characteristics, and task requirements, as well as strategies stored in long-term memory to assist task completion. Online awareness, on the other hand, occurs throughout a task and involves monitoring and regulation of performance. This involves anticipatory awareness (monitoring task demands) as well as emergent awareness (awareness of performance). Having accurate assessments of online awareness (i.e., accurate self-monitoring) is beneficial to individuals, as this provides information regarding when to engage in compensatory strategies (e.g., when presented with a large quantity of information, an individual takes notes as they have awareness of memory difficulties).

The majority of research examining self-awareness in pwMS has primarily sought to examine 'intellectual' awareness of cognitive abilities/impairments (Goverover, Chiaravalloti, Gaudino-Goering, Moore, & DeLuca, 2009). This is achieved through examining how 'intellectual' assessments of cognition (e.g., rating levels of cognitive difficulties experienced over the preceding four weeks) map onto 'actual' cognitive difficulties, assessed through standardised neuropsychological assessments (Goverover et al., 2009; Sherman, Rapport, & Ryan, 2008). These studies demonstrated negligible relationships between self-reported difficulties and actual performance on cognitive tasks.

Recent research, however, has examined both 'intellectual' and 'online' awareness of cognitive difficulties in pwMS. Specifically, Goverover et al. (2014) demonstrated that *online*, rather than *intellectual* assessment of cognitive performance was associated with actual performance. In this case, online awareness was inferred by the alignment between online reporting and actual task performance. Goverover et al. argued these results are likely to be due to intellectual measures reflecting individual's self-efficacy beliefs, whereas online measures are based off both self-efficacy and continual monitoring of performance. Interestingly, their study found that levels of online awareness did not differ between pwMS and controls. However, intellectual awareness was lower for pwMS, perhaps highlighting that pwMS may struggle to accurately rate the difficulties, as they occur over time, potentially due to poor memory (Brassington & Marsh, 1998) or depressed mood (Lovera, Bagert, Smoot, & Wild 2006). Importantly, these findings highlight two imperative points. Firstly, online and intellectual measures of performance are discrepant constructs. Secondly, online assessments are more consistent with actual

performance; therefore, the use of online measures may offer a more sensitive and ecologically valid method of assessing insight into difficulties.

The findings of Goverover et al. (2014) offer valuable information into other areas of self-awareness in pwMS. Specifically, many studies conducted into cognitive *fatigue* in pwMS, have found negligible relationships between objective and subjective measures of fatigue. However, these studies have typically relied on intellectual assessments (Morrow, Weinstock-Guttman, Munschauer, Hojnacki, & Benedict, 2009), which, if similar to intellectual awareness of cognitive abilities, may not accurately reflect cognitive fatigue. Through implementing both intellectual and online assessments, it may be possible to assess both intellectual and online awareness of cognitive fatigue. This can be achieved if self-report measures are compared to objective performance on cognitive tasks that are sensitive to the effects of fatigue (i.e., aligning self-report with objective measure).

Trait fatigue.

Trait fatigue refers to self-reported fatigue as is subjectively experienced over a period of time (i.e., 'intellectual' self-reports; Genova et al., 2013). Trait fatigue is viewed as being relatively stable, meaning it is not likely to drastically change over time. The Fatigue Impact Scale (FIS) developed for and validated in pwMS assesses trait fatigue (Fisk, Pontefract, Ritvo, Archibald, & Murray, 1994; Mathiowetz, 2003). This questionnaire asks participants to recall fatigue levels over the last four weeks. One important consideration of this measure in fatigue research is that it is not specific to cognitive fatigue. This is problematic because levels of cognitive fatigue can be experienced independently from levels of physical fatigue (Benedict et al., 2002; DeLuca, 2005). The Modified Fatigue Impact Scale (MFIS) addresses this problem by specifically examining various subtypes of fatigue, one of these being

cognitive fatigue (Ritvo et al., 1997). The MFIS has been employed to assess trait cognitive fatigue in pwMS (Tellez et al., 2005). However, measuring trait fatigue does not always align with the way that cognitive fatigue is objectively examined (i.e., assessing changes across a single session; Morrow et al., 2009). Therefore, claims into the relationships between subjective and objective fatigue are questionable.

Given the discrepancies between the temporal nature of the objective measurements, and the stable subjective measure (trait fatigue measures), it is unsurprising that negligible correlations have been discovered (Morrow et al., 2009). Trait measures may lack the sensitivity to assess changing fatigue across time. In order to assess the relationship between objective and subjective cognitive fatigue in a single session it would be practical to ask questions that relate to how the individuals are *currently* feeling (i.e., online awareness). This can be achieved by measuring state fatigue.

State fatigue.

Levels of state fatigue can be inferred through individuals 'online' self-reports. Given state fatigue allows for an 'online' assessment, it may have a stronger relationship with actual cognitive fatigue, in a similar manner to studies that have examined 'online' awareness of cognitive *abilities* (Goverover et al., 2014). Indeed, recent research has demonstrated that online measures, may be more sensitive to overly fatiguing tasks, in comparison to self-reported intellectual measures of fatigue (Genova et al., 2013). However, the extent to which these self-report measures are related to actual declines in objective performance remains unclear and requires further examination (Krupp & Elkins, 2000; Sandry et al., 2014). Examination of the extent pwMS evaluate declining cognitive performance (i.e., objectively assessed

cognitive fatigue) is important in order to gain an understanding of the nature of cognitive fatigue as it is appraised by pwMS.

Online awareness of cognitive fatigue is often obtained through use of a Visual Analogue Scale (VAS). In these scales, individuals are required to indicate how they feel on a scale of two extremes, 'not at all fatigued' to 'extremely fatigued'. A prevailing issue in the MS literature has been the use of a single question to assess an individual's online level of fatigue (Krupp & Elkins, 2000; Sandry et al., 2014). This limitation may be addressed through the use of the VAS to evaluate fatigue severity (VAS-F; Lee, Hicks, & Nino-Murcia, 1991). The VAS-F has 18 items where individuals rate their current levels of fatigue (and energy), thus it provides a more comprehensive account of the individual's experience. To date, however, there have been no studies to employ the VAS-F to assess 'online' reports of cognitive fatigue in relation to declining cognitive performance over time.

Objectively measuring fatigue

The objective assessment of cognitive fatigue has proven to be a challenging task (Sandry et al., 2014). Largely owing to this is the fact that fatigue is most commonly conceptualised as an *experience* or feeling that a person has about their levels of 'tiredness'. Nonetheless, several hypotheses have been proposed in the literature in an attempt to explain the mechanisms underlying the experience of *cognitive* fatigue in MS.

One proposed explanation of the experience cognitive fatigue is the *cognitive domain hypothesis* (Sandry et al., 2014). This hypothesis proposes that pwMS are more prone to deficits within particular cognitive domains (e.g., speed of processing and working memory, as opposed to knowledge of words; Benedict et al., 2002). As a consequence, when tasks require them to utilise these affected domains, psMS will

experience fatigue, as a result of expending more resources (Sandry et al., 2014). Whilst this hypothesis has good theoretical justifications, to date, there is a lack of empirical support for this.

Another proposed hypothesis is the *cognitive load hypothesis*. This theory suggests that cognitively demanding tasks are more likely to result in fatigue (Sandry et al., 2014). However, empirical support for this theory is also lacking. One study that has attempted to examine this in pwMS was conducted by Bailey, Channon, and Beaumont (2007), where the *n*-back task was employed, and manipulated to increase the level of cognitive load (i.e., 0-back to one 1-back task). Both the 0-back and 1-back tasks were administered twice to see changes across the individual test and across repeated administration. Findings suggested, irrespective of cognitive load, performance decreased temporally. In the 0-back, decreases in performance were observed across the single administration, whereas, in the 1-back, decreases in performance were not observed until the second administration. As Bailey et al. did not directly compare performance between the 0-back and 1-back tasks claims relating to fatigue due to cognitive load are questionable. Given that decreased performance was present across both the 'low' and 'high' load. The findings may more accurately align with the temporal hypothesis.

The *temporal hypothesis* suggests that fatigue is secondary to cognitive impairments, and in particular, slowed processing speed and attentional impairments (Andreasen, Spliid, Andersen, & Jakobsen, 2010). The basic premise is that as a result of these impairments, individuals need to employ more neural resources than healthy individuals to complete the same tasks (Andreasen et al., 2010). This can lead to decreased performance on tasks that require sustained mental effort (Sandry et al., 2014). Initial support for the temporal hypothesis can be observed by a study

conducted by Krupp and Elkins (2000) who measured declining performance over time by repeating tests in the same testing session. It was found that, whereas performance of control participants improved across the testing session, pwMS declined. More recently, Sandry et al. (2014) simultaneously examined the three fatigue hypotheses (cognitive domain, cognitive load and temporal hypothesis) and found the greatest support for the temporal fatigue hypothesis. They found, consistent with Bailey et al. (2007), cognitive fatigue increased as a result of sustained mental effort to the task (i.e., performance was poorer during later runs), regardless of cognitive load. Importantly, these three studies provided justification that performance over time may be a plausible means of quantifying the experience of fatigue in pwMS.

These studies have predominantly relied on standard neuropsychological test batteries. However, given that the temporal hypothesis proposes that fatigue is a secondary result of slowed processing speed and attentional impairments; measures confounded by other factors (e.g., cognitive load, or cognitive domain) may impact the validity of assessing this hypothesis. Potentially a more appropriate way to assess the temporal hypothesis may be through a measure of sustained attention. Therefore, given the inconsistencies of studies that have implemented standard neuropsychological tests, the current study employed the Conners Continuous Performance Test - 3 (CPT-3). This includes a measure of sustained attention. It is proposed that, should the temporal hypothesis hold true, the CPT-3 will detect changes in accuracy and response time across both a single administrations and across repeated testing in the same session.

The Relationship Between the Temporal Hypothesis and Subjective Fatigue.

The three studies mentioned above (Bailey et al., 2007; Krupp & Elkins,

2000; Sandry et al. 2014) also attempt to assess the relationship between objective and subjective cognitive fatigue. All studies found non-significant correlations between deteriorating performance and 'online' assessments of fatigue. However, all studies shared the same limitation preventing confidence in interpretation of their conclusions; only a single item was used to assess subjective fatigue. Furthering this, the question Bailey et al. (2007) employed was not specific to cognitive fatigue. Of these studies both Krupp and Elkins (2000), and Bailey et al. attained a measure of intellectual assessment; the Fatigue Severity Scale (Krupp et al., 1989), which also was uncorrelated objective performance. Whilst these studies attempted to assess the relationship between subjective and objective measures, this was in respect to correlational relationships. Specifically, it was not of the interest of these papers to examine awareness of fatigue (i.e., the alignment between the subjective reports and objective performance). Therefore, awareness of cognitive fatigue remains an area of research that is yet to be examined.

Aims and Hypotheses

The current study aimed to further examine the relationship between the subjective experience of cognitive fatigue and objectively measured cognitive fatigue by improving on the methodological flaws of past research (Krupp & Elkins, 2000; Sandry et al., 2014). This will be achieved by employing reliable and valid methods of assessing both *state* and *trait* self-reported cognitive fatigue to predict performance on an objective test of sustained attention (CPT-3) that is administered twice in the same testing session. Finally, the current study aims to explore awareness into fatigue by examining match between both self-reported trait and state cognitive fatigue and objectively measured cognitive fatigue. The aims of the current study will allow for a more thorough examination of the nature of fatigue and how

this may be experienced in pwMS.

In line with prior research demonstrating cognitive impairments in pwMS (Bagert, Camplair, & Bourdette, 2002; Brassington & Marsh, 1998), it was hypothesised that pwMS would have poorer scores on the neuropsychological tests, compared to the demographically matched healthy control participants (HC). Secondly, based on high prevalence rates of cognitive fatigue in pwMS (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989), it was hypothesised that pwMS would have higher self-reported scores on the MFIS and VAS-F in comparison to the HC sample. Further, consistent with the findings of Krupp and Elkins (2000), it was hypothesised that pwMS, but not HC participants, will demonstrate decreased performance on the sustained attention measures on the second administration of the CPT-3, in comparison to the first administration (i.e., there will be a significant interaction). It was also hypothesised that 'online' assessment of cognitive fatigue (state fatigue) rather than 'intellectual' assessment of cognitive fatigue (trait fatigue) will be predictive of objective cognitive fatigue. Hence providing support for the notion that intellectual and online awareness of fatigue are indeed separate constructs that need to be examined more thoroughly in future research. Finally, based on the work of Goverover et al. (2014) who found that awareness of cognitive abilities were only impaired (i.e., overestimations of impairment) for pwMS in respect to their intellectual, but not online self-assessments, it was hypothesised that levels of intellectual awareness of fatigue, but not online awareness of fatigue, will differ between pwMS and HC.

Method

Participants

Participants included 31 pwMS and 30 HC (for demographic data see Table 1). The average disease duration for pwMS was 11 years (*SD* = 8 years), the disease characteristics of which are presented in Table 2. A higher ratio of females was attained, as this is reflective of higher prevalence of MS amongst females (Harbo et al., 2013). Overall, the proportion of females to males did not differ between the groups (χ^2 = .26, *p* = .613). An a priori power analysis conducted using G*Power (version 3.1.9.2; Faul, Erdfelder, Lang, & Buchner, 2007) indicated that a sample size of 46 participants would be required in order to obtain a large effect size for deteriorating test performance across time (*d* =.75, alpha level = .05, power =.80; based on the results from Krupp and Elkins, 2000).

The MS participants were primarily recruited by direct invitation through a letter sent to participants of the Australian Multiple Sclerosis Longitudinal Study (AMSLS) managed by the Menzies Institute of Medical Research (Appendix B). Additionally, participants were recruited by referral through the MS Society of Tasmania, local MS neurologists and health professionals, and advertisements placed on the MS Society of Tasmania Facebook page. HC participants were recruited through advertising on the University of Tasmania's Newnham Campus noticeboards and advertisement on personal Facebook pages (advisement material shown in Appendix C).

Table 1

Participant Demographic Characteristics

	MS	HC			
Demographics	*M* (*SD*)	*M* (*SD*)	*t* (59)	*p*	Cohens *d*
Female	22 (37%)	23 (36%)			
Male	9 (14%)	7 (11%)			
Age	47.77 (12.19)	44.37 (11.37)	-1.13	.264	.29
Education	12.13 (1.57)	12.87 (1.91)	1.65	.105	.42
Intelligence	102.87 (5.27)	104.38 (5.27)	1.16	.252	.29
Anxiety	7.42 (4.33)	5.87 (2.94)	-1.64[#]	.108[#]	.42
Depression	6.10 (3.36)	3.10 (3.16)	-3.59	.001	.92

Note. Frequency values for gender are shown and parenthesis indicate percentages of the overall sample; An estimation of premorbid intelligence was calculated based on the formula developed by Barona, Reynolds, and Chastain (1984); [#]Equal variance not assumed statistic reported; Additional analyses revealed the significant difference in depression did not account for between group difference observed in other analyses (see Appendix D for analyses).

Table 2

Participant Disease Characteristics

Type of MS	*n*
Relapsing Remitting	22 (73%)
Secondary Progressive	2 (7%)
Primary Progressive	5 (17%)
Relapsing Progressive	1 (3%)

Note. MS-type is self-reported. Percentages of MS sample are shown in brackets.

Participants were excluded from the study if any of the following were present: (1) not aged between 18 and 65 years; (2) a diagnosis of a psychotic, bipolar or related disorder; (3) a history of brain injury or other neurological illness (e.g., stroke, epilepsy); (4) a history of alcohol or illicit drug abuse; (5) unable to speak and read English fluently; (6) uncorrected visual difficulties; and (7) were pregnant. Additional exclusion criterion for pwMS was a disease relapse (symptom flare-up) within the two weeks preceding assessment. For pwMS, a diagnosis of clinically definite MS as defined by the McDonald criteria (Polman et al., 2011) was required.

Design

The study employed a cross-sectional design to examine the relationship between objective and subjective measures of cognitive fatigue in pwMS. Additionally a within-subjects design to examine changing self-reported cognitive fatigue and cognitive performance over the course of a testing session was utilised.

Materials

Self- Report Questionnaires.

Demographic questions. Demographic questions relating to individuals' age, gender, and years of education were completed in a self-report survey.

Hospital Anxiety and Depression Scale (HADS). The HADS (Zigmond & Snaith, 1983) is a 14-item questionnaire that assesses current levels of *depression* and *anxiety*, with 7-items forming both a depression and an anxiety subscale. Participants are required to respond to each item (e.g., 'I feel tense or 'wound up") on a 4-point scale: 0 (little symptom occurrence) to 3 (higher symptom occurrence). Subscale scores range from 0–21, with higher scores indicative of higher symptomology. Severity levels are specified by the following: normal (0–7), mild (8–10), moderate (11–14) or severe (15–21). The scale avoids reliance on symptomatic aspects of depression and anxiety that may also be common with the neurovegetative symptoms of MS (e.g., fatigue). The HADS has high levels of internal consistency for the depression and anxiety subscales (Cronbach's α=.94 and .92, respectively; Honarmand & Feinstein, 2009), and high test-retest reliability over a 3-week period (r = .91; Spinhoven et al., 1997). The HADS was utilised in as prior research indicates a relationship between depression and fatigue (Bakshi et al., 2000).

Modified Fatigue Impact Scale (MFIS). The MFIS was developed for clinicians and researchers and forms part of the MS Quality of Life Survey (Ritvo et al., 1997). The 21-item scale comprises of three subscales: physical, cognitive and psychosocial. Items are rated using a Likert type scale, with response options ranging from 0 (never) to 4 (almost always), higher scores indicating more severe fatigue. For the purpose of the study, the cognitive subscale items were used (10 items; score range = 0-40). The MFIS has excellent internal consistency (Cronbach's α = .93;

Ritvo et al., 1997), and good test-rest reliability over a 6-month period (r = .86; Learmonth et al., 2013).

Visual Analogue Scale – Fatigue (VAS-F). The VAS-F (Lee, Hicks, & Nino-Murcia, 199) is an 18-item self-report scale, which asks participants to rate their *current* levels of fatigue (13-items) and energy (5-items) between two extreme indictors of occurrence (e.g., 'Not at all tired' to 'Extremely tired'). The scale has excellent internal consistency in both healthy individuals and individuals with sleeping disorders (Cronbach's α above .91), and demonstrates good discrimination from self-reported measures of mood (Lee et al., 1991). Energy items are reversed, giving an overall fatigue score.

Neuropsychological Tests.

The Brief Repeatable Neuropsychological Battery (BRNB; Rao, 1990), specifically developed to assess cognitive functioning in MS was administered. This battery comprises of the tests mentioned below. Forms A and B of the tests were implemented.

Selective Reminding Test (SRT). The SRT (Buschke, 1973) was employed to assess unstructured verbal learning and memory. A list of 12 unrelated words are read to participants, who are then asked to recall the words in any sequence. The participants are then read the words they missed, and again asked to recall the *entire* list. There are a total of five learning trials. Following a 15 to 25-minute delay, participants are asked to recall the list again. The SRT has been found to have good internal consistency (Cronbach's α above .85; Grober, Ocepek-Welikson, & Teresi, 2009), and has previously been validated for use in MS populations (Beatty et al., 1996). The SRT assesses both short (the total number of words recalled across the six learning trials) and long-term memory (total delayed recall).

10/36 Spatial Recognition Test (SPART). The SPART (Rao, 1990) is a test of visuospatial learning and memory. Participants view a 6×6 (25×25cm) grid with 10 black circles in specific locations for 10 seconds. The marked grid is then replaced with a blank grid and participants are required to replicate the pattern. The test is completed three times using the same pattern. Following 15 to 25-minute delay, the participant is asked to recreate the pattern again, this assess LTM. Test-retest reliability is high for the immediate recall task, however is only adequate for the delayed recall (ICC *r* = .85 and .57, respectively; as measured on three occasions over 18-months; Portaccio et al., 2010) Scores are calculated based on the correct responses across the three learning trials, and the delayed total.

Paced Serial Addition Test (PASAT). The PASAT (Gornwall, 1977) assesses working memory, divided attention, and information processing speed. Single digit numbers are presented to the participant via voice recording. Participants are instructed to provide verbal responses of the sum of two consecutive digits for the entire sequence of digits. The test involves two trials, each with 60 numbers; the first trail has 3-second intervals between digits and the second trial has 2-second intervals. The PASAT has high internal consistency (Cronbach's α above .91; Crawford, Obonsawin & Allan, 1998) and high test-retest reliability over a three-month period (Spearman's correlation = .80; Sjøgren, Thomsen & Olsen, 2000). Scores are based on the correct number of responses across the two trials.

Symbol Digits Modality Test (SDMT). The SDMT (Smith, 1982) assesses sustained attention, visual scanning and tracking. Using a reference key comprising of nine geometric symbols labeled from 1 to 9, the examinee has 90 seconds to verbally pair a number with the corresponding symbol. The SDMT, has high concurrent validity with the Digit Symbol subtest of the WAIS (*r* = .75-.85; Morgan

& Wheelock, 1992), and has high test-retest over a one-month period (Spearman correlation = .80; Benedict et al., 2008). Scores on this test are the total number of correct number-symbol pairs.

Verbal Fluency Task. The Verbal Fluency task (Rao, 1990) assesses verbal generation ability. Participants are asked to generate as many words as possible starting with a particular letter of the alphabet in 60 seconds. The participants complete three letter trials (Form A = F, O, J; Form B = A, N, V). Participants are instructed not to use the same word with different endings (e.g., sip, sipped, sipping), numbers (e.g., seventy, seventy one), or words that ordinarily begin with a capital letter (e.g., names of places and people). Parallel versions of this test demonstrate very good internal consistency in mixed clinical samples (Strauss, Sherman, & Spreen, 2006). The verbal fluency task has high test-retest reliability over an 18-month period (ICC = .85; Portaccio et al., 2010). Scores are calculated on the total number of correct words across the three letter trails.

Additional neuropsychological tests administered to accompany the BRNB include the following.

Weschler Memory Scale 4th Edition: *Logical Memory I and II (WMS-IV LMI and LMII).* The LM tasks (Wechsler & Drozdick, 2009) assesse structured verbal memory. Short stories are presented orally to participants, who are required to immediately recall the story. Following a period of approximately 20 minutes, participants are asked to recall the story. The LM tasks forms part of the Wechsler Memory Scale, which has been found to have excellent internal consistency (r =.83-.97) and high test-retest reliability over 14-84 days (r = .81; The British Psychological Society, 2012). Scores are calculated based on the number of correct details recalled for the immediate trail, and for delayed trial.

Conners Continuous Performance Test – 3 (CPT–3). The CPT-3 (Conners, 2014) is a computerised task to assess attention difficulties. This test was used in the current study to measure objective cognitive fatigue. Indices in the test include measures of inattentiveness, vigilance, and sustained attention. Measures of inattentiveness (commission and omission errors) and sustained attention will specifically be used in this study. The task requires participants to press the space bar every time they see a letter on the computer screen, except the letter "X", where they are asked to not provide a response and wait for the next letter to appear. Time intervals between letter presentations vary (1, 2 and 4 seconds) throughout the 14-minute test. The task is a valid tool, not for only ADHD populations, but also assessing attention deficits that may be secondary to other disorders (Conners, 2014). The CPT-3 has good test-retest reliability following a one-week delay (.70-.90 for the various indices; Conners, 2014). Sustained attention is a combination of the rates of omissions (measured by missed targets), commissions (measured by responding to a non-target) as well as hit reaction time (HRT; measured by changes in reaction across time) across the 14-minute trial. The CPT-3 produces *t*-scores for the three above indices with higher scores being indicative of poorer performance.

Procedure

Prospective participants contacted the researchers to complete a screening interview (Appendix E), which ensured eligibility and to arrange a mutual time to complete testing, at either the University of Tasmania Newnham or Burnie Campus. Eligible participants were sent a package containing a letter confirming testing details, an information sheet, and consent form (Appendix F). A hard copy of the survey was sent to participants or made available online through SurveyMonkey. Participants were asked to complete the survey 1-7 days prior to their assessment.

The day prior to testing, participants were phoned to confirm their attendance. At this time, disease relapse status of the participants was checked according to the guidelines of Brown et al. (2006; Appendix G). A relapse in the past 2 weeks resulted in rescheduling of the testing session. Prior to giving informed consent the details of the study were verbally discussed and participants were required to read the information sheet to ensure they understood the requirements of the study. All participants were advised, both at screening and at interview, that they were free to withdraw from the study at any stage without consequence.

Participants were tested in the morning to control for time of day effects associated with fatigue. A brief interview was conducted immediately prior to testing to obtain basic details relevant to disease status and medical history (Appendix H). Additional information was obtained regarding age and date of disease onset, type of MS. The testing session took between 92 and 178 minutes to complete. Test order and test forms were counterbalanced across participants to minimise any possible order effects, this resulted in four test batteries (Table 3 contains test battery A and B, battery C and D are presented in Appendix I). Important for the present study, was the administration of the CPT-3 test, which at Time 1 occurred on average 35 minutes (*SD* = 5-minutes) into the testing session and Time 2 occurred on average at 113 minutes (*SD* = 17-minutes). Also important was the administration of the VAS-F at Baseline (prior to the administration of the first neuropsychological test), Time 1 (immediately post CPT-3 Time 1), and Time 2 (immediately post CPT-3 Time 2). Tests were administered in accordance with the manual's standardised instructions. All participants who partook in the study received $60 remuneration for their time.

Estimation of missing scores. Five pwMS were unable to complete the 2-sec trial of the PASAT (i.e., they were significantly impaired on the task). Where this

occurred, scores were estimated based on *z*-score performance of the 3-sec trial of the task. Specifically, *z*-scores were calculated for the HC data for the 3 and 2 second trial. Using this normative data, *z*-scores were then calculated for impaired participants' 3-sec trial performance. This *z*-score was then used to estimate performance on the 2-sec trial using the normative information (i.e., the z-score was substituted into the formula: $M - (z\text{-score} \times SD)$).

Cognitive Impairment Status. Additional analyses were conducted to examine if subjective fatigue was dependent on cognitive impairment. Cognitive impairment was determined according to ninth percentile cut-off scores, based on the normative data obtained from the HC. Individuals were classified as being impaired if they scored below the ninth percentile on two or more tests. This resulted in 17 pwMS being classified as cognitively impaired.

Calculating discrepancy scores. An estimation of intellectual and online awareness was obtained by calculating discrepancy scores between the self-report and objective fatigue measures (i.e., CPT-3 indices). This was achieved by transforming raw scores for the subjective measures (MFIS and VAS-F) and objective fatigue (CPT-3 HRT and commission) measures to *z*-scores (based on the overall sample). When analysing objective fatigue in relation to trait subjective fatigue (to assess intellectual awareness), the second administration of the CPT-3 was used. This was because the second administration of the CPT-3 was most likely to be indicative of a state of fatigue and would better resemble the fatigue that may be induced by undertaking everyday activities. Discrepancy scores were calculated by subtracting the *z*-scores of self-reported fatigue measures away from the CPT-3 *z*-scores (e.g., Time 1 CPT-3 HRT *z*-score minus Time 1 VAS-F *z*-score). Negative scores represent over-estimation of self-reported fatigue relative to objectively

measured performance, whereas positive scores represent an under-estimation of self-reported fatigue.

Statistical Analysis

Data were analysed using SPSS version 23. Alpha levels were maintained at .05 for all analyses to determine significant effects. Effect sizes for analyses were calculated and interpreted in accordance to Cohen's recommendations (Cohen, 1992). Specifically, for Cohen's *d* .20 indicates a small effect, .50 a moderate effect and .80 a large effect. Partial eta-squared (η^2) values were interpreted for omnibus tests of significance, where .01 was representative of a small effect, .09 a medium effect and .25 a large effect. Correlations were interpreted as .1 is a small effect, .3 is a medium effect and .5 is a large effect. Additionally, the magnitude of the regression analyses (R^2) were interpreted by the recommendation Ferguson (2009), whereby, .04 as a minimum interpretable effect, .25 as a moderate effect and .64 as a strong effect. For the Mann-Whitney U analysis the effect size was calculated in accordance with the recommendations of Fritz, Morris, and Richler (2012) using the formula: $r = z/\sqrt{N}$ (*r*-values interpreted in accordance with Cohen, 1992).

Table 3

Neuropsychological Tests Version A and B.

Test Battery	Approximate Time (min)
1. Visual Analogue Scale - Fatigue	3-5
2. Selective Reminding Test	8-10
3. Logical Memory Test	3-5
4. 10/36 Spatial Recognition Test	5-7
5. Symbol Digits Modality Test	3
6. Paced Serial Addition Test	10-12
7. Selective Reminding Test – Delayed Recall Trial	1-2
8. Logical Memory Test – Delayed Recall Trial	1-2
9. 10/36 Spatial Recognition Test – Delayed Recall Trial	1-2
10. Verbal Fluency task	4-5
11. Conners Continuous Performance Test – 3 (CPT-3)	16
12. Visual Analogue Scale - Fatigue	2-3
13. The Awareness of Social Inference Test - Short (TASIT-S)*	25-30
SHORT BREAK (5-10 MINS)	
14. Selective Reminding Test	8-10
15. Logical Memory Test	3-5
16. 10/36 Spatial Recognition Test	5-7
17. Symbol Digits Modality Test	3
18. Paced Serial Addition Test	10-12
19. Selective Reminding Test – Delayed Recall Trial	1-2
20. Logical Memory Test – Delayed Recall Trial	1-2
21. 10/36 Spatial Recognition Test – Delated Recall Trial	1-2
22. Verbal Fluency Task	3
23. Conners Continuous Performance Test – 3	14
24. Visual Analogue Scale - Fatigue	2-3

Note. Form A was utilised for the first half of the testing in version A and Form B first for version B. *The Awareness of Social Inference Test – Short (TASIT-S) and the second half of the test battery will be published in separate papers.

Data Screening

Prior to analyses being conducted, data screening was performed. Several variables were detected as having a moderate positive skew (verbal fluency, the CPT-3; HRT administration two, and omissions administration one and two), based on a calculated normed skewness statistic greater than 3.29 (Tabachnick & Fidell, 2013). All variables were square root transformed which normalised the distribution of the variables and reduced the frequencies of outliers. Analyses were then conducted using both the raw data and the transformed data. Given that the use of transformed data had no impact on the results (Appendix J), for ease of interpretation, all results presented in this paper are bases on the raw data (Appendix K).

The current study employed a range of statistical methods to interpret the results. A series of independent *t*-tests were conducted to examine the differences between pwMS and the HC on: demographic data, age, education, estimated full scale intelligence, anxiety and depression. Additional Analyses were conducted to determine if depression was significantly altering the findings between-group findings., the first administration of the neuropsychological tests, and MFIS scores.

Mixed factorial ANOVAs with group as the between subject's variables were conducted to examine changes in the VAS, and changes across the three measures of the CPT-3 (HRT, commissions, omissions). As omissions did not differ between groups, the remainder of the analysis only examined HRT and commissions. ANOVAs were followed up with both independent sample *t*-tests and paired samples *t*-tests. Independent samples *t*-tests were also conducted to detect between group differences on insight scores. However, due to a violation of homogeneity of variance in the independent samples *t*-test examining insight based on HRT Time 2

and VAS-F Time 2 scores, a Mann-Whitney U non-parametric analysis was conducted. Finally, four regression analyses were conducted to examine ability of both state (VAS-2 or VAS-3) and trait (MFIS) subjective fatigue measures to predict performance on the objective measures of fatigue (HRT and commissions).

Results

Baseline Neuropsychological tests

The results from the first administration of the neuropsychological tests revealed that pwMS were significantly impaired on a range of tests (SRT, LM, SDM, PASAT, and both SRT and LM delayed), in comparison to the HC. Table 4 provides an overview of test performance for each group.

Objective Cognitive Fatigue

Hit Response Time (HRT). The results from the 2 (group) × 2 (time) mixed factorial ANOVA demonstrated no main effect for group on HRT, $F(1, 59) = 1.80$, $p = .185$, $\eta^2 = .03$. That is, overall performance between and pwMS ($M = 53.08$, $SD = 7.84$) and HC ($M = 50.38$, $SD = 7.85$) did not differ. There was also no significant main effect of time, $F(1, 59) = .00$, $p = .982$, $\eta^2 = .00$, with HRT at Time 1 ($M = 51.75$, $SD = 9.11$) being equivalent to HRT at Time 2 ($M = 51.72$, $SD = 10.26$). However, there was a significant interaction between group and time, $F(1, 59) = 7.50$, $p = .008$, $\eta^2 = .18$ (see Figure 5). Post-hoc examinations were conducted using independent samples *t*-tests and paired samples *t*-tests. Specifically, independent samples *t*-tests revealed that there was no difference at Time 1, $t(59) = .56$, $p = .578$, $d = .14$. However, at Time 2, pwMS performed significantly poorer than HC, $t(59) = -2.55$, $p = .013$, $d = .14$. In addition, paired samples *t*-tests indicated there was not a significant change in performance for pwMS across time, $t(30) = -1.63$, $p = .115$, $d = .40$. However, HC performance significantly improved across time $t(29) = 2.57$, $p = .015$, $d = .43$.

Table 4

Mean scores on the neuropsychological tests.

	MS			HC					
		95% CI			95% CI				
Test	*M (SD)*	*LL*	*UL*	*M (SD)*	*LL*	*UL*	*t*	*p*	Cohens *d*
SRT - Total Recall	46.32 (12.01)	41.92	50.73	52.43 (8.98)	49.08	55.79	2.24	.028	.58
LM	10.26 (3.16)	9.10	11.42	12.86 (3.71)	11.48	14.25	2.96	.004	.82
10/36 - Total	19.94 (4.80)	18.18	21.69	21.30 (5.80)	19.13	23.47	1.00	.320	.26
SDM	47.39 (9.94)	43.73	51.03	59.17 (10.80)	55.14	63.20	4.44	<.001	1.14
PASAT	74.10 (22.54)	65.83	82.36	85.17 (17.03)	78.80	91.52	2.16	.035	.55
SRT – Delayed	6.74 (2.86)	5.69	7.79	8.70 (2.51)	7.77	9.67	2.84	.006	.73
LM – Delayed	8.55 (3.34)	7.33	9.77	11.93 (4.03)	10.43	13.44	3.58	.001	.92
10/36 Test – Delayed	7.10 (2.15)	6.31	7.89	7.40 (2.03)	6.64	8.16	.57	.573	.14
Verbal Fluency	28.10 (10.35)	24.92	32.50	32.53 (11.11)	28.39	36.82	1.39	.169	.41

Note. CI = confidence interval; LL = lower limit; UL = upper limit.

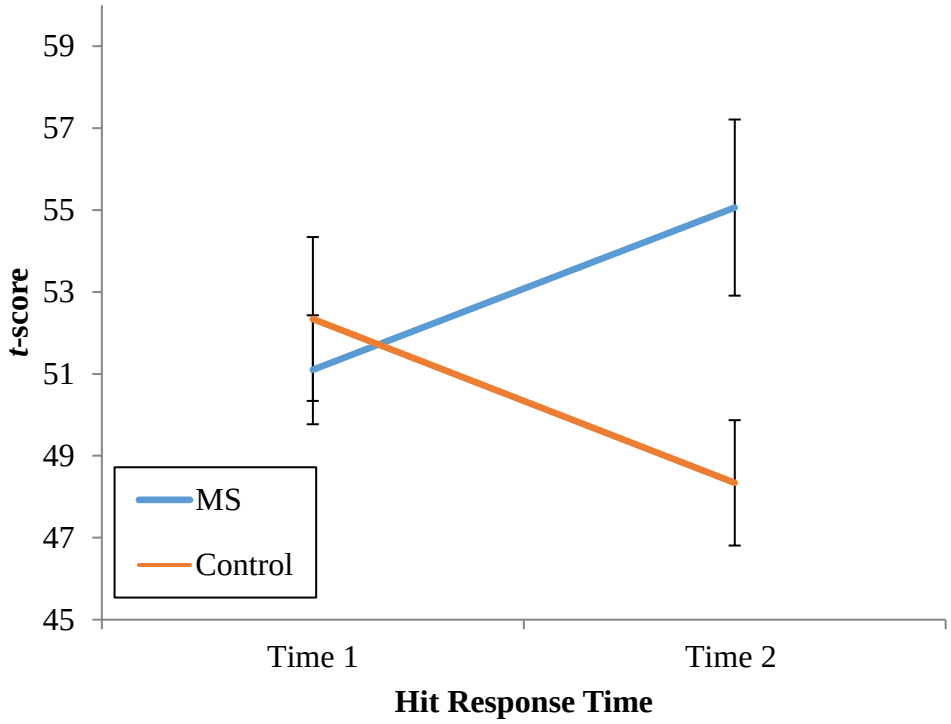

Figure 5. Interaction between group and hit response time across time session on the CPT-3 task. Higher *t*-scores represent poorer performance. Error bars represent standard errors.

Commissions. The results from the 2 (group) × 2 (time) mixed factorial ANOVA demonstrated pwMS ($M = 53.77$, $SD = 8.36$) had more commission errors than HC ($M = 48.58$, $SD = 8.36$), $F(1, 59) = 5.88$, $p = .018$, $\eta^2 = .09$. There was also a main effect of time, with commission rates being higher at Time 1 ($M = 50.60$, $SD = 8.36$) than Time 2 ($M = 51.76$, $SD = 8.95$), $F(1, 59) = 4.06$, $p = .050$, $\eta^2 = .06$. Furthermore, there was a significant interaction between group and time, $F(1, 59) = 10.26$, $p = .002$, $\eta^2 = .15$ (see Figure 6). To further examine this relationship, post-hoc independent samples *t*-tests were conducted. While no group differences at Time 1 were detected [$t(59) = -1.55$, $p = .126$, $d = .14$], the MS participants had significantly more commission errors at Time 2 [$t(59) = -3.08$, $p = .003$, $d = .79$].

Paired samples *t*-tests indicated that whereas pwMS performance significantly decreased [$t(30) = 3.66$, $p = .001$, $d = .30$], HC performance did not change across time [$t(29) = .85$, $p = .400$, $d = .09$].

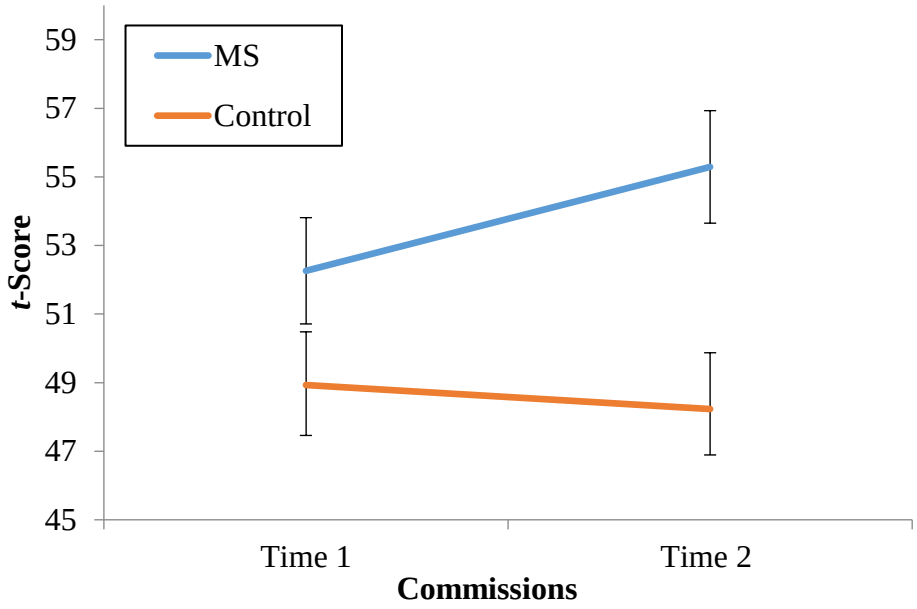

Figure 6. Interaction between group and commissions across sessions on the CPT-3 task. Higher *t*- score values represent poorer performance. Error bars represent standard errors.

Omissions. The 2 (group) × 2 (time) mixed factorial ANOVA indicated that there was no main effect of condition, $F(1, 59) = .28$, $p = .599$, $\eta^2 = .01$. That is, levels of omissions did not differ between pwMS ($M = 48.57$, $SD = 7.25$) and HC ($M = 47.58$, $SD = 7.25$). Further, omission rates did not differ from Time 1 ($M = 47.93$, $SD = 7.33$) to Time 2 ($M = 48.22$, $SD = 8.81$), $F(1, 59) = .10$, $p = .754$, $\eta^2 = .00$. There was also no significant interaction between group and time, $F(1, 59) = .04$, $p = .837$, $\eta^2 = .01$ (see Figure 7).

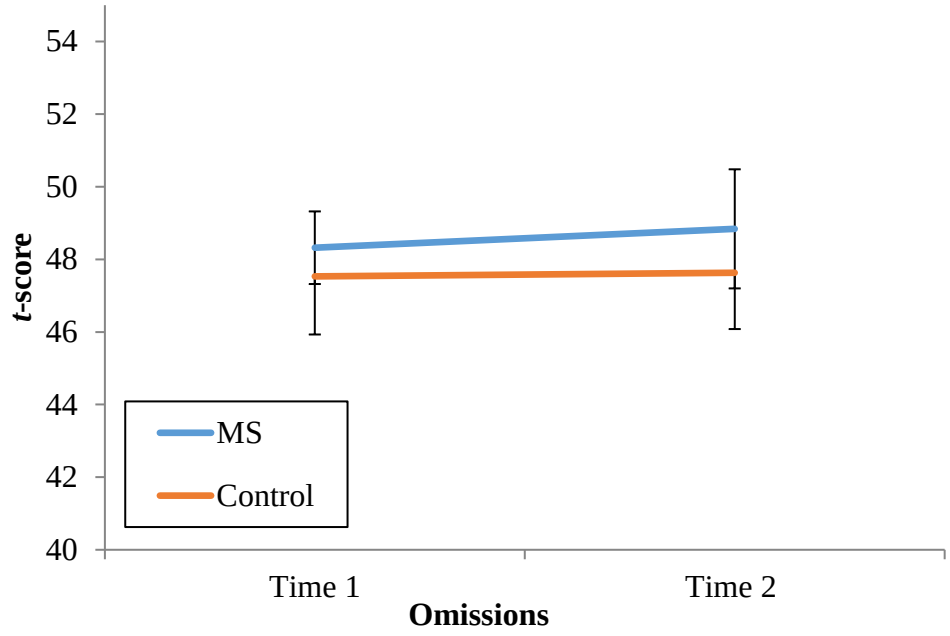

Figure 7. Interaction between group and omissions across sessions on the CPT-3 task. Higher *t*-score values represent poorer performance. Error bars represent standard errors.

Subjective Cognitive Fatigue

An independent samples *t*-test demonstrated pwMS (*M* = 15.58, *SD* = 7.32) had higher self-reported trait fatigue (assessed using the MFIS) in comparison to HC (*M* = 9.67, *SD* = 5.09), *t*(59) = -3.65, *p* = -3.65, *d* = .94.

A 2 (group) × 3 (time) mixed factorial ANOVA with VAS-F scores as the dependent variable, revealed a significant main effect of condition. Specifically, pwMS (*M* = 90.40, *SD* = 28.82) reported more fatigue than HC (*M* = 53.08, *SD* = 28.81), *F*(1, 59) = 25.57, *p* <.001, η^2 = .30. There was also a significant main effect of time [*F*(1.18, 93.11) = 63.59, *p* < .001, η^2 = .52], indicating there were differences between Baseline (*M* = 53.43, *SD* = 31.41) and Time 1 (*M* = 71.54, *SD* = 37.84) [*t*(60) = 5.40, *p* < .001, *d* = .51]. Time 1 also differed from Time 2 (*M* = 91.15, *SD* =

42.59), [$t(60) = 7.72$, $p < .001$, $d = .47$].

The interaction revealed Mauchly's test of sphericity was violated ($\chi^2(2) = 18.04$, $p < .001$, $\varepsilon = .79$), therefore, adjusted degrees of freedom were interpreted (Greenhouse-Geisser correction). A significant interaction between group and time was present $F(1.58, 93.11) = 4.80$, $p = .016$, $\eta^2 = .08$ (Figure 8). Independent samples *t*-tests revealed pwMS had higher self-reported ratings of fatigue than HC, this was consistent across Baseline [$t(59) = -3.60$, $p = .001$, $d = .90$], Time 1 [$t(59) = -4.61$, $p < .001$, $d = 1.17$], and Time 2 [$t(59) = -5.13$, $p < .001$, $d = 1.30$]. Furthermore, paired samples *t*-tests indicated VAS-F scores for pwMS and HC increased from Baseline to Time 1 [$t(30) = 4.82$, $p < .001$, $d = .73$; $t(29) = 2.81$, $p = .009$, $d = .46$ respectively], and from Time 1 to Time 2 [$t(30) = 7.54$, $p < .001$, $d = .64$; $t(29) = 3.92$, $p < .001$, $d = .36$, respectively].

Subjective fatigue predicting objectively measured fatigue

Results from the four multiple regressions with the MFIS and VAS-F self-report measures of fatigue predicting actual performance on the CPT-3 are presented in Table 5. The only model found to be significant was the regression for Time 2 self-report measures predicting CPT-3 commission errors. Within this model, only the VAS-F scores were found to significantly predict individual variance (15%) in commission errors. A moderate positive zero-order correlation was also found between the MFIS and commission errors at Time 2, and a large positive zero-order correlation for the VAS-F at Time 2. Moderate positive zero-order correlations were found between the two self-report measures and the commission errors at Time 1.

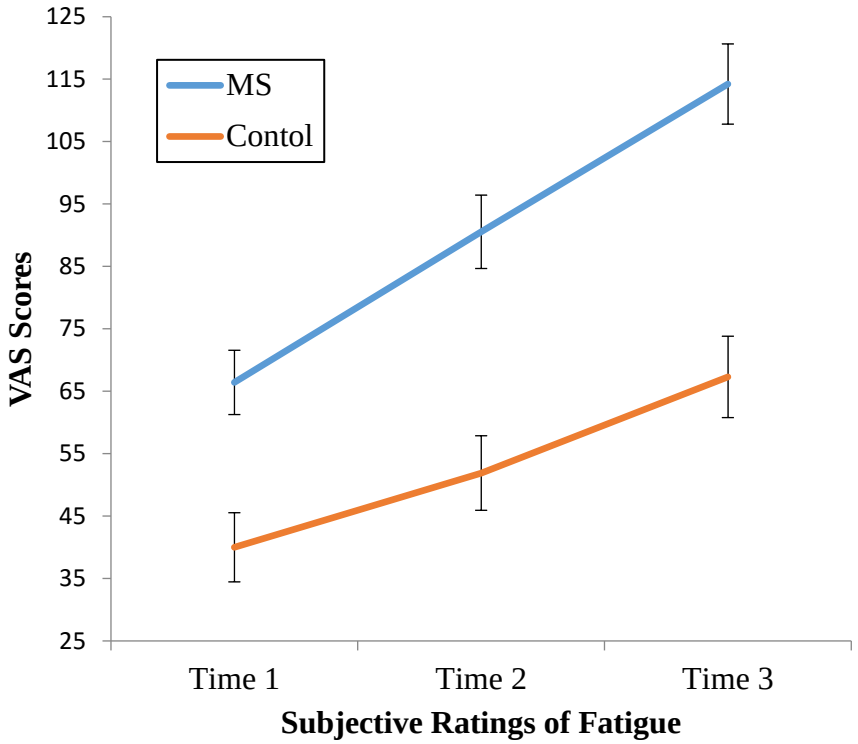

Figure 8. Interaction between group and VAS-F ratings. Higher VAS-F values represent greater self-reported fatigue. Error bars represent standard errors.

Assessing insight into fatigue using discrepancy scores

When examining discrepancy scores it was found that at Time 1 of the CPT-3, pwMS reported significantly higher levels of fatigue relative to actual performance (i.e., over-reporting fatigue), compared to HC (Table 6 presents means and inferential statistics). Due to the violation of homogeneity of variance in the HRT-VAS-F discrepancy score at Time 2, a Mann-Whitney analysis was conducted. The results demonstrated a trend towards over-reporting subjective fatigue (relative to actual performance on CPT-3 HRT) in pwMS (Mdn = 35.40) relative to HC (Mdn = 26.74), $U = 333.00$, $p = .057$, $r = -.24$. All other comparisons of insight revealed no significant differences between pwMS and HC ($p > .05$).

Table 5

Regression Analyses Examining the Predictive Ability of Subjective Measures of Fatigue on Objective Fatigue.

	Dependent Variables												
	HRT							Commissions					
						95% *CI*						95% *CI*	
	R^2	*r*	β	sr^2	*B*	*LL*	*UL*	R^2	*r*	β	sr^2	*B*	*LL*	*UL*
Time 1	.05							.10						
VAS-F		-.10	-.17	.02	-.03	-.12	.06		.27	.20	.04	.05	-.05	.14
MFIS		.14	.20	.04	.20	-.20	.61		.26	.19	.03	.22	-.24	.68
Time 2	.06							.23*						
VAS-F		-.18	-.22	.03	-.07	-.20	.06		.44*	.39	.15	.11	.01	.21
MFIS		.12	.19	.05	.30	-.33	.94		.29	.19	.03	.27	-.23	.76

Note. Zero-order correlations were interpreted according to the guidelines of Cohen (1992).

* $p < .05$

Cognitive Fatigue Stratified by Cognitive Impairments

Additional *t*-test analyses were conducted to examine whether fatigue in pwMS differed due to cognitive impairment status (impaired compared to not impaired). Analyses revealed no significant differences between groups on the three objective measures of cognitive fatigue (HRT, commissions and omissions), self-report measures of fatigue, and insight into fatigue (results for these analyses are presented in Appendix L).

Table 6

Comparisons of Levels of Insight Between pwMS and HC.

	MS	HC			
	M (SD)	*M (SD)*	*t*(59)	*p*	Cohens *d*
Time 1: CPT-3 – VAS-F					
HRT	-.57 (1.36)	.59 (1.21)	3.54	.001	.90
Commissions	-.31 (1.23)	.32 (1.23)	2.00	.050	.51
Time 2: CPT-3 – VAS-F					
HRT	-.23 (1.51)	.24 (.88)	1.50[#]	–	–
Commissions	-.18 (1.04)	.18 (1.09)	1.34	.186	.34
Time 2: CPT-3 – MFIS					
HRT	-.11 (1.43)	.12 (.90)	.74	.462	.14
Commissions	-.06 (1.27)	.06 (.92)	.40	.690	.11

Note. Means and standard deviations are of the *z*-scores; [#]Indicates a violation of homogeneity of variance, therefore significance and effect sizes are not interpreted.

Discussion

One primary aim of this study was to improve on the existing literature by furthering current understandings regarding objectively measured cognitive fatigue and its relationship with self-reported cognitive fatigue. The first hypothesis, that pwMS would demonstrate poorer performance on the neuropsychological tests, compared to the control sample, was partially supported. Consistent with previous research (Sepulcre et al., 2006), the current study found that pwMS were impaired in the following domains of cognition; structured and unstructured verbal memory, sustained and divided attention, working memory and processing speed, and long-term memory. However, there were no observable differences in verbal fluency, or visuospatial learning or delayed recall. Chiaravalloti and DeLuca (2008) report that impairments in verbal fluency are one of the least common impairments, affecting approximately 15 percent of pwMS, however, impairments to visual memory affect over 50 percent of pwMS. This may indicate that levels of impairments in the present study may be smaller than prior research.

The hypothesis that pwMS would have higher self-reported ratings of subjective state and trait cognitive fatigue than healthy participants, as indicated by scores on the VAS-F and MFIS, was supported. In particular, the current study found that pwMS reported significantly higher levels of *state* fatigue across all administrations of the VAS-F. This is consistent with both prior research (Sandry et al., 2014) and the notion that fatigue increases in response to particular tasks, or as the day progresses (Branas et al., 2000). Furthermore, pwMS also reported higher levels of *trait* fatigue, in comparison to healthy participants. This is indicative of the general and persistent experience of cognitive fatigue amongst pwMS (Branas et al., 2000).

Prior literature states that there is a temporal basis to the experience of cognitive fatigue (Sandry et al., 2014). This study aimed to directly test this theory by hypothesising that pwMS, but not healthy participants, would perform more poorly on repeated assessment of sustained attention (CPT-3), relative to an initial assessment within the same testing session. The study found support for the temporal hypothesis based on the following: (1) in pwMS there was a more pronounced reaction time change (i.e., slowing reaction time across the 14-minute test administration) in the second administration of the sustained attention task relative to the first administration; (2) There were increased errors of commission in pwMS in the second administration of the sustained attention task relative to the first administration. These findings are further discussed below.

In respect to reaction time, while no significant difference between groups were detected on the first administration of the sustained attention task, significant difference between the groups were detected on the second administration. Specifically, while the performance of healthy participants improved, the performance of pwMS did not change. It is notable, that the effect size for this change in pwMS was small to medium (d = .40), which was similar to the effect size seen in the control participants (d = .43). This suggests that a possible meaningful decrease was observed in pwMS, but not detected due to lack of power. The non-significant relationship may also have been attributable to the larger variation observed in pwMS (SD = 12.60), in comparison to HC (SD = 8.60). The results are consistent with prior research, demonstrating pwMS experienced a decrease in performance, whereas, controls experienced an increase in performance on standardised neuropsychological tests administered over the course of a single testing session (Krupp & Elkins, 2000).

Similar to the reaction time performance noted above, while there were no differences observed between groups commission rates on the first administration, at the second administration pwMS had significantly more errors of commission than the healthy control participants. Specifically, pwMS had more commissions in the second administration relative to the first, whereas, controls performance remained consistent. While this finding supports the hypothesis that pwMS will experience declines in performance across testing sessions, it does not support the hypothesis that control participants will improve across testing. To summarise, however, present study supports the notion that pwMS do indeed experience significant declines in performance over a single testing session in line with the temporal theory of cognitive fatigue.

The results from the current study provide partial support for the hypothesis that 'online' assessment (i.e., using a measure of *state* fatigue), rather than 'intellectual' assessment (i.e., using a measure of *trait* fatigue) of cognitive fatigue will predict objective cognitive fatigue. Here it was found that the self-reported cognitive fatigue predicted 23 percent of the variance in scores on the second administration of the sustained attention task. However, this was only in respect to errors of commissions. Of the two subjective measures, the 'online' assessment measure was the only unique predictor. Online assessment also had a large zero-order correlation with commission errors at this time. While further regression modelling with the self-report measures as predictors were not significant, moderate positive correlations were detected between the intellectual assessment of fatigue and both reaction time and commission errors, and the online assessment of fatigue and reaction time, at the second administration. These results provide support for the notion that 'online' and 'intellectual' assessments of fatigue are separate constructs,

which should be examined independently. While online assessments of fatigue appear to be most advantageous in predicting actual cognitive fatigue, where their use is impractical, intellectual assessment may serve as a reasonable alternative.

The current study found no group differences in levels of intellectual awareness of cognitive fatigue, thus finding no support for the final hypothesis that a group difference would exist in intellectual awareness. This result is not consistent with the findings of Goverover et al. (2014) who found that intellectual awareness of *cognitive ability* was lower in pwMS than healthy control participants (i.e., pwMS had a tendency to over-report fatigue levels relative to controls). Intellectual assessment of fatigue requires a participant to reflect on their experience of fatigue over the past four weeks, and thus relies on memory to accurately report levels of fatigue. The similar levels of insight between pwMS and healthy control participants suggest pwMS are well able to remember experiences of fatigue.

The current study found mixed results when examining online awareness in pwMS. At the first administration of the sustained attention task, online awareness of cognitive fatigue differed between pwMS and healthy controls. In particular, whereas pwMS tended to overestimate their experience of cognitive fatigue, healthy control participants tended to underestimate it. However, following the second administration of the task, arguably after a state of cognitive fatigue was present (as indicated by increased commission errors and poorer HRT); online awareness did not differ significantly between groups. There was, however, a trend towards pwMS overestimating their experience cognitive fatigue, as assessed by the discrepancy between self-reported state fatigue and reaction time.

The results obtained when examining awareness provide support for the use of *intellectual* measures. Intellectual measures may be viewed as having more utility

in clinical practice due to the ease of administration. Nonetheless, where possible these measures should be supplemented with 'online' measures, as they offer greater predictive ability. In respect to intellectual measures, previous research has indicated that subjective *trait* measures offer an invaluable source of information into how an individual perceives their abilities, and that these perceptions can be more influential than actual abilities (Honan et al., 2015). In this respect, perceptions can influence the way individuals behave. Therefore, it is important to understand that the consideration of only objective, state or trait fatigue does not fully encompass the experience of cognitive fatigue in pwMS. Future research should endeavour to uncover the extent to which the various measures of cognitive fatigue relate to functional outcomes.

A final finding of this current study is that cognitive fatigue was not influenced by cognitive impairment. That is, individuals who were classified as having impairments did not experience significantly more (or less) cognitive fatigue than pwMS not classified with impairments. This supports prior literature that claims fatigue can be experienced independently from other impediments (Benedict et al., 2002; DeLuca, 2005).

The findings from the current study provide valuable information into understanding the nature of the cognitive fatigue that pwMS experience. The measures of the sustained attention on the CPT-3 assessed different aspects of cognition. It was found that the 'online' assessment of cognitive fatigue was predictive of commission errors. However, it was also found that reaction time increases temporally; however, subjective ratings were not predictive of this. This suggests that current subjective measures that assess 'online' cognitive fatigue are not sensitive to the varying dimensions of cognitive fatigue. Future research may

endeavour to identify domains where fatigue is objectively observable and, subsequently, develop measures of cognitive fatigue that relate to the various domains. However, given cognitive fatigue has demonstrated to be multifaceted it may be challenging to develop measures that can encapsulate the full phenomenon.

Study Limitations

The results of the current study should be interpreted in view of the following limitations. In the current study, as well as in past research, depression symptomology was higher in the MS participants. The current study did not fully examine the role that depression may have played in the relationship between subjective and objective cognitive fatigue. This was in part due to the fact that overall depression levels of pwMS were in the normal range (i.e., below a score of 7). Nonetheless, alternative analyses with depression included as a covariate did not change the present results. However, it remains possible that depressive symptomology may mediate the relationship between subjective and objective cognitive fatigue for pwMS. This can be examined in a future larger study that has more power to detect significant relationships in mediation-type analyses (Fritz & MacKinnon, 2007).

A further limitation that should be taken into consideration is that the study was conducted in winter and employed a restrictive sample from North and North West Tasmanian. As it is common for pwMS to be affected by heat (Davis & Jacobson, 1971), therefore, the results from this study may have differed if the study was conducted in warmer climates or during warmer months.

Conclusion

The majority of pwMS experience and live with cognitive fatigue on a daily basis. This study provided the ability to objectively assess cognitive fatigue by

examining declining performance across time on a task of sustained attention, the CPT-3. Furthermore, increases in subjective reports of cognitive fatigue were also examined, both providing support for the temporal hypothesis. The current study provides greater insight into the relationship between subjective and objectively measured fatigue. Specifically, the employment of the VAS-F and the CPT-3, can be viewed as a large improvement in the literature on fatigue, as it was through these measures a relationship between the subjective and objective cognitive fatigue was uncovered. The study highlights the importance of attaining 'online' assessments in both clinical and experimental practices. Due to the absence of effective measures for assessing subjective cognitive fatigue, it is recommended that both subjective (trait, and where possible, state) and objective measures should be taken. The study concludes with the recommendation that future research should attempt to develop a VAS that can more thoroughly encompass the multifaceted phenomenon of fatigue.

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Appendix A

Ethics Approval

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HUMAN RESEARCH ETHICS COMMITTEE (TASMANIA) NETWORK

UTAS

03 June 2016

Dr Cynthia Honan
C/o UTAS - Psychology

Sent via email

Dear Dr Honan

REF NO: H0015630
TITLE: Fatigue in multiple sclerosis: An examination of the construct, its relationship with everyday functioning and biomarkers

Document	***Version***	***Date***
Application Form - NEAF	-	-
Protocol – MS and Fatigue Study Final Honan et al	2.0	-

The Tasmanian Health and Medical Human Research Ethics Committee considered and approved the above documentation on **01 June 2016** to be conducted at the following site(s):

University of Tasmania

Please ensure that all investigators involved with this project have cited the approved versions of the documents listed within this letter and use only these versions in conducting this research project.

This approval constitutes ethical clearance by the Health and Medical HREC. The decision and authority to commence the associated research may be dependent on factors beyond the remit of the ethics review process. For example, your research may need ethics clearance from other organisations or review by your research governance coordinator or Head of Department. It is your responsibility to find out if the approvals of other bodies or authorities are required. It is recommended that the proposed research should not commence until you have satisfied these requirements.

All committees operating under the Human Research Ethics Committee (Tasmania) Network are registered and required to comply with the *National Statement on the Ethical Conduct in Human Research* (NHMRC 2007 updated 2014).

Therefore, the Chief Investigator's responsibility is to ensure that:

(1) The individual researcher's protocol complies with the HREC approved protocol.

(2) Modifications to the protocol do not proceed until **approval** is obtained in writing from the HREC. Please note that all requests for changes to approved documents must include a version number and date when submitted for review by the HREC.

(3) Section 5.5.3 of the National Statement states:

Researchers have a significant responsibility in monitoring approved research as they are in the best position to observe any adverse events or unexpected outcomes. They should report such events or outcomes promptly to the relevant institution/s and ethical review body/ies and take prompt steps to deal with any unexpected risks.

The appropriate forms for reporting such events in relation to clinical and non-clinical trials and innovations can be located at the website below. All adverse events must be reported regardless of whether or not the event, in your opinion, is a direct effect of the therapeutic goods being tested. http://www.utas.edu.au/research-admin/research-integrity-and-ethics-unit-rieu/human-ethics/human-research-ethics-review-process/health-and-medical-hrec/managing-your-approved-project

(4) All research participants must be provided with the current Patient Information Sheet and Consent Form, unless otherwise approved by the Committee.

(5) The Committee is notified if any investigators are added to, or cease involvement with, the project.

(6) This study has approval for four years contingent upon annual review. A *Progress Report* is to be provided on the anniversary date of your approval. Your first report is due **01 June 2017.** You will be sent a courtesy reminder closer to this due date.

(7) A *Final Report* and a copy of the published material, either in full or abstract, must be provided at the end of the project.

Should you have any queries please do not hesitate to contact me on (03) 6226 2764.

Yours sincerely

Heather Vail
Ethics Administrator
Office of Research Services
Email: Heather.vail@utas.edu.au
University of Tasmania
Private Bag 01 Hobart Tas 7001

Appendix B

Recruitment Letter

UNIVERSITY of TASMANIA | FACULTY OF HEALTH

1st July 2016

Dear AMSLS Participant,

Invitation to Participate in Research

Cognitive Fatigue in Multiple Sclerosis

I am writing to invite you to participate in a research study currently being conducted in Launceston and Burnie examining fatigue and potential new biomarkers of fatigue in people with multiple sclerosis. The research is being funded by and conducted in collaboration with Multiple Sclerosis Research Australia. This letter has kindly been sent to you on my behalf by Assoc. Professor Ingrid van der Mei (Manager of the Australian MS Longitudinal Study and Senior Epidemiologist at the Menzies Institute) as a potential person who might be interested in participating in this additional research.

Your participation will provide us with some invaluable information about your experience of fatigue, that will inturn assist other people with MS, researchers, and clinicians who work with people with MS, to further understand the types of fatigue-related factors which are most relevant in predicting everyday social functioning. This understanding may also lead to more effective rehabilitative and medicinal treatment programs for those who experience difficulties with fatigue as a result of their MS.

I have enclosed a flyer and "Information for Participants" sheet for you to read. If after having read the information you would like to participate, you can express your interest by either phoning me directly on 03 6324 3266 or by emailing me at cynthia.honan@utas.edu.au.

Many thanks for your consideration in participating in this study and I very much look forward to hearing from you. If you have any questions or concerns, please do not hesitate to contact me.

Yours sincerely,

Dr Cynthia Honan
Lecturer and Clinical Neuropsychologist

Appendix C

Recruitment Advertisement

MS & Fatigue Study

Call for Research Participants

We are looking for volunteers with Multiple Sclerosis or healthy individuals without MS to take part in study investigating fatigue, everyday social functioning and biomarkers of fatigue and haemostasis.

As a participant, you will be asked to complete a **questionnaire**, undertake a **brief interview**, undertake some face-to-face **assessment tasks**, and undertake a **blood test**. The questionnaire should take no longer than 1 hr and the interview/tasks no longer than 3 hours to complete.

You will be reimbursed **$60** for your participation.

To volunteer or for further information please contact:

Dr Cynthia Honan

Lecturer and Clinical Neuropsychologist

Discipline of Psychology, School of Medicine, Faculty of Health

University of Tasmania

Ph: 03 6324 3266 or

Email: cynthia.honan@utas.edu.au

This study is being funded by **Multiple Sclerosis Research Australia** and has been approved by the Tasmanian Health and Medical Human Research Ethics Committee.

Appendix D

Between Group Analyses with Depression as a covariate

Between-Subjects Factors

		Value Label	N
Type(1-ctr)	1.0	CTRL	30
	2.0	MS	31

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.
Intercept	Pillai's Trace	.964	171.275[b]	8.000	51.000	.000
	Wilks' Lambda	.036	171.275[b]	8.000	51.000	.000
	Hotelling's Trace	26.867	171.275[b]	8.000	51.000	.000
	Roy's Largest Root	26.867	171.275[b]	8.000	51.000	.000
Depression	Pillai's Trace	.241	2.028[b]	8.000	51.000	.061
	Wilks' Lambda	.759	2.028[b]	8.000	51.000	.061
	Hotelling's Trace	.318	2.028[b]	8.000	51.000	.061
	Roy's Largest Root	.318	2.028[b]	8.000	51.000	.061
Type1ctr	Pillai's Trace	.370	3.747[b]	8.000	51.000	.002
	Wilks' Lambda	.630	3.747[b]	8.000	51.000	.002
	Hotelling's Trace	.588	3.747[b]	8.000	51.000	.002
	Roy's Largest Root	.588	3.747[b]	8.000	51.000	.002

a. Design: Intercept + Depression + Type1ctr

b. Exact statistic

Tests of Between-Subjects Effects

Source	Dependent Variable	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	VAS-F_1	15355.215[a]	2	7677.608	10.157	.000
	HRT1	32.322[b]	2	16.161	.192	.826
	Con(1)_IN(Com)	191.258[c]	2	95.629	1.352	.267
	VAS-F_2	28603.488[d]	2	14301.744	14.471	.000
	HRT2	843.401[e]	2	421.701	4.040	.023
	Con(2)_IN(Com)	881.054[f]	2	440.527	5.547	.006
	VAS_F(3)	38383.223[g]	2	19191.611	15.798	.000
	COM_INSIGHT_VAS3	2.243[h]	2	1.122	.983	.380
	HRT_INSIGHT_VAS3	11.345[i]	2	5.673	3.947	.025
	HRT_INSIGHT_MFIS	15.205[j]	2	7.603	6.249	.003
	COM_INSIGHT_MFIS	2.345[k]	2	1.173	.959	.389
	HRT1_Inshight_VAS2	23.721[l]	2	11.860	7.274	.002
	HRT1_Inshight_MFIS	20.600[m]	2	10.300	6.817	.002
Intercept	VAS-F_1	32910.053	1	32910.053	43.538	.000
	HRT1	52493.577	1	52493.577	623.199	.000
	Con(1)_IN(Com)	49343.521	1	49343.521	697.508	.000
	VAS-F_2	65319.747	1	65319.747	66.095	.000
	HRT2	58276.186	1	58276.186	558.368	.000
	Con(2)_IN(Com)	49374.146	1	49374.146	621.738	.000
	VAS_F(3)	121527.184	1	121527.184	100.039	.000
	COM_INSIGHT_VAS3	.162	1	.162	.142	.708
	HRT_INSIGHT_VAS3	5.379	1	5.379	3.742	.058
	HRT_INSIGHT_MFIS	9.750	1	9.750	8.014	.006
	COM_INSIGHT_MFIS	1.454	1	1.454	1.188	.280
	HRT1_Inshight_VAS2	2.155	1	2.155	1.322	.255
	HRT1_Inshight_MFIS	3.822	1	3.822	2.529	.117
Depression	VAS-F_1	4713.846	1	4713.846	6.236	.015
	HRT1	6.429	1	6.429	.076	.783
	Con(1)_IN(Com)	22.732	1	22.732	.321	.573
	VAS-F_2	5830.717	1	5830.717	5.900	.018
	HRT2	159.452	1	159.452	1.528	.221
	Con(2)_IN(Com)	121.791	1	121.791	1.534	.221
	VAS_F(3)	4811.270	1	4811.270	3.961	.051
	COM_INSIGHT_VAS3	.225	1	.225	.197	.659
	HRT_INSIGHT_VAS3	7.876	1	7.876	5.479	.023
	HRT_INSIGHT_MFIS	14.416	1	14.416	11.849	.001
	COM_INSIGHT_MFIS	2.146	1	2.146	1.754	.191
	HRT1_Inshight_VAS2	3.020	1	3.020	1.852	.179
	HRT1_Inshight_MFIS	5.471	1	5.471	3.621	.062

Type1ctr	VAS-F_1	4147.751	1	4147.751	5.487	.023
	HRT1	32.302	1	32.302	.383	.538
	Con(1)_IN(Com)	94.940	1	94.940	1.342	.251
	VAS-F_2	10900.430	1	10900.430	11.030	.002
	HRT2	843.263	1	843.263	8.080	.006
	Con(2)_IN(Com)	411.852	1	411.852	5.186	.026
	VAS_F(3)	18672.813	1	18672.813	15.371	.000
	COM_INSIGHT_VAS3	1.180	1	1.180	1.034	.313
	HRT_INSIGHT_VAS3	.250	1	.250	.174	.678
	HRT_INSIGHT_MFIS	.644	1	.644	.529	.470
	COM_INSIGHT_MFIS	.047	1	.047	.038	.846
	HRT1_Inshight_VAS2	11.470	1	11.470	7.034	.010
	HRT1_Inshight_MFIS	6.422	1	6.422	4.250	.044
Error	VAS-F_1	43841.703	58	755.891		
	HRT1	4885.481	58	84.232		
	Con(1)_IN(Com)	4103.070	58	70.743		
	VAS-F_2	57319.660	58	988.270		
	HRT2	6053.386	58	104.369		
	Con(2)_IN(Com)	4605.963	58	79.413		
	VAS_F(3)	70458.450	58	1214.801		
	COM_INSIGHT_VAS3	66.195	58	1.141		
	HRT_INSIGHT_VAS3	83.365	58	1.437		
	HRT_INSIGHT_MFIS	70.564	58	1.217		
	COM_INSIGHT_MFIS	70.960	58	1.223		
	HRT1_Inshight_VAS2	94.571	58	1.631		
	HRT1_Inshight_MFIS	87.629	58	1.511		
Total	VAS-F_1	233313.000	61			
	HRT1	168202.000	61			
	Con(1)_IN(Com)	160618.000	61			
	VAS-F_2	398128.000	61			
	HRT2	170388.000	61			
	Con(2)_IN(Com)	169289.000	61			
	VAS_F(3)	615622.000	61			
	COM_INSIGHT_VAS3	68.438	61			
	HRT_INSIGHT_VAS3	94.710	61			
	HRT_INSIGHT_MFIS	85.769	61			
	COM_INSIGHT_MFIS	73.305	61			
	HRT1_Inshight_VAS2	118.292	61			
	HRT1_Inshight_MFIS	108.229	61			

Corrected Total	VAS-F_1	59196.918	60			
	HRT1	4917.803	60			
	Con(1)_IN(Com)	4294.328	60			
	VAS-F_2	85923.148	60			
	HRT2	6896.787	60			
	Con(2)_IN(Com)	5487.016	60			
	VAS_F(3)	108841.672	60			
	COM_INSIGHT_VAS3	68.438	60			
	HRT_INSIGHT_VAS3	94.710	60			
	HRT_INSIGHT_MFIS	85.769	60			
	COM_INSIGHT_MFIS	73.305	60			
	HRT1_Inshight_VAS2	118.292	60			
	HRT1_Inshight_MFIS	108.229	60			

Appendix E

Screening Interview

SCREENING INTERVIEW

The following screening interview will be conducted over the phone with the potential participant. Upon contact, the participant will be provided with information about the study as follows:

Information about the study

1. Provide description of the topic under investigation and purpose of the project (similar to what is provided in the information sheet).
2. Specify that it involves completion of a questionnaire (40-60 mins), taking a blood & urine test (5 mins), undertaking a brief interview (10-15 mins) and undertaking some assessment tasks (2 hrs 15 mins to 2 hours 45 mins). Indicate the types of tasks that will be undertaken (assess memory, attention, vigilance, verbal fluency, reasoning, information processing, and social functioning). Also advise that we would like to contact a family member or friend to ask a few questions about their social functioning.
3. Discuss voluntary participation, right to withdraw at any time.
4. Discuss Anonymous participation and confidentiality.
5. Discuss potential risks (fatigue due to testing, possible bruising due to blood test)
6. Outline the benefits of the research generally. Also specify that they will not directly benefit from the research.
7. Discuss reimbursement of $60.
8. Advise that will be asked to eat breakfast prior to attending the assessment session.

Screening Questions

The individual will then be asked if they mind being asked some quick questions to assess your eligibility to participate in the study. They will be advised that some of the questions will enquire about their medical history. They will be assured that all information will be kept confidential and this screening questionnaire will be securely destroyed at the conclusion of your participation.

The following screening questions will be asked:

Age: _____ (if aged under 18 years or over 65 years, individual is excluded)

Are you able to read and speak English? Y / N (if no, individual is excluded)

Do you have any uncorrected visual difficulties? Y / N

If yes, provide details? _____

(Researcher to make decision about whether visual difficulties would prevent individual from validly completing tasks)

Do you have a diagnosis of a psychotic, bipolar or related disorder? _____

Do you have a history of brain injury or other neurological illness? _____

Do you have a history of alcohol or illicit drug abuse? _____

Are you pregnant? _____

(if yes to any of the above questions, individual is excluded)

The following additional questions will be asked only to individuals with MS:

Is your MS diagnosis verifiable by your treating neurologist? _____

When did you last experience a relapse or flare up of MS symptoms? _____
(if within the past 2 weeks the participant is excluded from the study)

Additional questions

These are additional questions to ensure that they are able to fully participate in the study.

Will you be prepared to undertake a blood & urine test? Y / N

Are you prone to any adverse reactions from undertaking a blood test (e.g., fainting, nausea/vomiting, convulsions) Y / N

Will you allow permission to contact a significant other so that we can ask them a few questions about their social functioning? Y / N

Will you be able to complete the survey form and undertake assessment tasks? Y / N

Are you able to attend a testing session at the University? Y / N

Do you have any difficulties with mobility and/or transportation? Y / N

(If yes, note details and discuss taxi requirements)

Do you have any further questions about the research? Y / N

(If participant satisfies selection criteria) Will you be willing to participate in the study?

Final Comments

If it is apparent to the researcher that the participant is severely cognitively impaired (this will be apparent as it will be difficult for them to answer questions or provide rational responses to questions), the individual will be excluded from the study.

If the individual doesn't satisfy the selection criteria they will be told that on this occasion they do not meet the criteria for this particular study. The individual will be thanked for their time.

If the individual does meet the selection criteria and is willing to participate obtain the following details:

Name: _____ Address: _____

Phone: _____ Email: _____

Ask the individual about their preferred days for a testing session: M / T / W / T / F

Advise the individual that they will shortly receive a telephone call from Caitlin Turner who will arrange a testing session with them and who will arrange for a full information sheet and consent form along with the survey form to be sent to them. Ask that they read the information sheet prior to providing consent, and where required have a "significant other" or carer also sign the consent form.

Appendix F

Information Sheet

Discipline of Psychology, School of Medicine
University of Tasmania

Participant Information Sheet

Fatigue in multiple sclerosis: An examination of the construct, its relationship with everyday functioning and biomarkers

April, 2016

Introduction

You are invited to participate in a study that examines the nature of fatigue and its relationship to potential new biomarkers and blood haemostasis. The research is being conducted by Dr Cynthia Honan, Dr Murray Adams, Dr Kiran Ahuja and Dr Edwin Lim (Macquarie University). Miss Caitlin Turner and Ms Sarah Harms will be assisting with the project in partial fulfilment of the requirements of an Honours degree in psychology. Caitlin and Sarah are being supervised by Dr Cynthia Honan from the School of Medicine, University of Tasmania. The researchers can be contacted as following: Dr Cynthia Honan (cynthia.honan@utas.edu.au; + 61 3 6324 3266); Dr Murray Adams (murray.adams@utas.edu.au; + 61 3 6324 5483); Dr Kiran Ahuja (kiran.ahuja@utas.edu.au; + 61 3 6324 5478); Dr Edwin Lim (edwin.lim@mq.edu.au); Caitlin Turner (caitlin.turner@utas.edu.au); Sarah Harms (sjharms@utas.edu.au)

Purpose of the study

The purpose of this study is to investigate the relationship between subjectively experienced fatigue, objectively measured fatigue (performance on thinking tasks over the duration of a testing session), everyday social functioning and social participation, and potential new biomarkers of fatigue and blood haemostasis in people with multiple sclerosis when compared to healthy individuals.

What does my participation involve?

If you wish to take part in this study, you will be asked some initial screening questions aimed at identifying whether you are suitable to participate. If you are deemed suitable, you will then be asked to sign the Participant Consent Form. After signing the consent form, you will be asked to complete a participant survey form which contains a series of questions related to your: (1) general background; (2) MS symptoms (if you have MS); (3) diet; (4) alcohol use; (5) symptoms of depression; (6) experience of fatigue; (7) experience of daytime sleepiness; (8) sleep quality; (9) perceived thinking difficulties; (10) social functioning; (11) social support; and (12) social participation. The survey is estimated to take between 40 minutes and 1 hour to complete. The completed questionnaire can be handed to the researchers or sent to:

Dr Cynthia Honan
Psychology, School of Medicine
University of Tasmania, Newnham Campus
Launceston TAS 7258

Following survey completion, you will attend a testing session where a blood sample will be taken and where you will undertake some tasks that assess your skills in memory, attention, vigilance, reasoning, information processing, and social functioning. In this session you will also complete short questionnaires to assess your present levels of fatigue. Completion of these tasks and the fatigue questionnaire, is estimated to take between 2 hrs 15 mins and 2 hrs 45 minutes to complete. You will also be briefly interviewed to obtain details of your medical history (e.g., any neurological illness, other health issues, medications). The interview is expected to take 10-15 minutes. Please ensure you eat breakfast prior to attending your testing session.

We will also ask you for permission to contact a family member or friend to complete a short survey about your social functioning.

Risks

There is little or no risk associated with your participation in this study. However, you may start to feel tired or fatigued during the testing session. Should this fatigue become excessive and you do not wish to continue, please advise the researcher. It is also possible that you may experience some bruising at the site of blood extraction. If you are prone to fainting when seeing blood or when undergoing blood tests, please ensure you advise the researchers.

Benefits

The current research is intended to improve our understanding of the nature of fatigue and the link that fatigue may have with important biomarkers, and blood haemostasis in MS. Whilst the benefits of participating in this research may not be of direct benefit to you, your participation will provide us with some invaluable information that will assist other people with MS, researchers, and clinicians who work with people with MS to further understand in particular the types of fatigue-related factors which are most relevant in predicting everyday social functioning. Such an understanding is important as it may lead to more effective rehabilitative medicinal treatment programs for those who experience difficulties with fatigue as a result of their MS.

You may be able to obtain the results of your neuropsychological testing at the request of your Psychology Board of Australia endorsed clinical neuropsychologist. Please contact your neuropsychologist to discuss obtaining these results. Dr Cynthia Honan (endorsed clinical neuropsychologist) will also be able to provide some brief verbal feedback on your neuropsychological results. Please contact Dr Honan to arrange a separate time for this feedback. Note that your individual results from the questionnaires that you complete and your blood test results will not be available.

Recompense to Participants

Participants will be reimbursed $60 at the conclusion of the testing sessions as recompense for their time. Participants who do not complete the full study may be offered a partial reimbursement for participation depending on the number of neuropsychological tests completed. Parking costs may be incurred (approx. 70c per hour). If you have limited mobility and/or no access to transport, a taxi may be arranged for you (at the expense of the researcher).

Voluntary Participation

Participation in this study is entirely voluntary. You do not have to take part in it. If you do take part, you can withdraw at any time without having to give a reason. Whatever your decision, please be

assured that it will not affect your relationship with the researchers or any other medical personnel. Only the researchers named above will be aware of your participation or non-participation.

Confidentiality

All the information collected from you for the study including all medical history and results will be treated confidentially, and only the researchers named above will have access to it. The results of this study may be presented at a conference or in a scientific publication, but individual participants will not be identifiable.

Further Information

When you have read this information, Dr Honan will discuss it with you further and answer any questions you may have. If you would like to know more at any stage, please feel free to contact Dr Honan on 03 6324 3266 or cynthia.honan@utas.edu.au.

How do I find out the results of the study?

A summary of the results will be made available on the Multiple Sclerosis Research Australia website (www.msra.org.au). Results of the overall study can also be obtained by contacting Dr Honan on 03 6324 3266 or cynthia.honan@utas.edu.au.

Ethics Approval and Complaints

This study has been approved by the Tasmanian Health and Medical Human Research Ethics Committee. If you have concerns or complaints about the conduct of this study should contact the Executive Officer of the HREC (Tasmania) Network on (03) 6226 7479 or email human.ethics@utas.edu.au. The Executive Officer is the person nominated to receive complaints from research participants. You will need to quote ???. Any complaint you make will be treated in confidence and investigated.

Who do I contact if I wish to speak to someone about my mental health?

As aforementioned, a number of questions will be asked about psychological functioning and alcohol and other drug use. Whilst it is not anticipated that these questionnaires will cause distress, please do not hesitate to let the researcher know if you do not wish to fill them in. If you are concerned about your mental health, please contact Lifeline 13 11 14, the Tasmanian Alcohol Drug Information Service 1800 811 994 or the MS Society of Tasmania 1800 676 721.

Consent Form

Discipline of Psychology, School of Medicine
University of Tasmania

PARTICIPANT CONSENT FORM

Fatigue in multiple sclerosis: An examination of the construct, its relationship with everyday functioning and biomarkers

1. I acknowledge that the nature, purpose and contemplated effects of the project so far as it affects me, have been fully explained to my satisfaction by the research worker and my consent is given voluntarily.
2. The details of the procedure proposed have also been explained to me, including the anticipated length of time it will take, the frequency with which the procedure will be performed, and an indication of any discomfort, which may be expected. I understand that my involvement means completing a survey (estimated time 40-60 min), undertaking an interview (10-15 min) and assessment tasks (up to approximately 2 hours 45 min), and a blood & urine test (5 min).
3. I understand that blood and urine samples will be taken in this study and that these samples will be stored for later analysis.
4. I understand that there are the following risks or discomfort: fatigue due to assessment tasks, possible bruising, and a minor risk of nausea or vomiting, fainting or convulsions as a result of the blood test.
5. Although I understand that the purpose of this study is to improve our understanding of fatigue and biomarkers in MS, leading to improved rehabilitation and treatment, it has also been explained that my involvement may not be of any benefit to me and that I will not be able to obtain my individual results from the researchers.
6. I have been given the opportunity to have a member of my family or a friend present while the project was being explained to me.
7. I am informed that no information regarding any medical history will be divulged and the results of any tests involving me will not be published so as to reveal my identity.
8. I understand that my involvement in the project will not affect my relationship with the researchers or the University of Tasmania. I also understand that I am free to withdraw from the study at any time and have my data and blood/urine sample not be included in the study.
9. I understand that I will be given a signed copy of the information sheet and consent form. I am not giving up my legal right by signing this consent form.
10. I understand that the trial will be conducted in accordance with the latest versions of the *National Statement on Ethical Conduct in Human Research 2007* and applicable privacy laws.

....	....
Signature of Participant Date	Signature of Witness * Date
.....	.....
(Please PRINT name)	(Please PRINT name)
....	.....
Signature(s) of Investigator(s) Date	Relationship to participant
.....	*The witness is not essential but will be required if the research team feel that the participant should have a witness to the consent procedure
Please PRINT Name	

Appendix G

Relapse Checklist

RELAPSE STATUS CHECKLIST (Part of Interview)

INSTRUCTIONS
The following sets of questions are to be ASKED BY THE RESEARCHER. That is, they do not form part of the questionnaire to be administered directly to people with MS. These questions ask for specific information about the neurological symptoms of the MS patient.

1. Have you had any relapse in the past 3 months? If yes, how many?	
2. Was the relapse a worsening of existing symptoms or new symptoms?	
3. How long did the symptoms last?	

4. In the past 3 months, which of the following symptoms have you suffered for 2 or more days?
(Note, reading this list is a means of jogging the memory of some patients who may have some cognitive impairment. Any such event or symptom must be lasting for >= 2 days)

	Neurological symptoms	**Present (✓) or absent (×)**
1	Difficulty walking/spasticity	
2	Incoordination/uncoordinated	
3	Weakness	
4	Numbness/tingling	
5	Pain	
6	Double vision/loss of vision	
7	Speech disturbances	
8	Bladder disturbances	
9	Bowel disturbances	
10	Other neurological disturbances	
11	Infection (fever, headache, cough, rhinitis, nausea/vomiting, diarrhoea,)	

Notes:

Appendix H

Interview for Ms participants

ID: _____ Date: _____

ABOUT YOUR MULTIPLE SCLEROSIS (MS) - INTERVIEW

1. Date of MS diagnosis	
2. Age at MS diagnosis	
3. Date when MS symptoms were first noticed	
4. MS type (e.g. relapsing/remitting, 2o progressive, primary progressive, relapsing progressive, benign, 1st demyelinating event)	
5. Current immunotherapy medications (e.g. β-feron, Avonex, Copaxone, Rebif, Tysabri)	
6. Immunotherapy details (when last used, for how long, frequency, dosage)	
7. Current other medications (e.g. prednisone [i.e. corticosteroids], antidepressants, tranquilisers, antiepileptics)	
8. Steroid medication details (In last 6 months: when, for how long, what type, dosage)	
9. Psychiatric illness (depression, anxiety disorders, schizophrenia)	
10. History of brain injury/neurological illness (e.g. TBI, MVA, alcoholism, epilepsy, stroke)	
11. Other health-related conditions (e.g. pregnancy, diabetes, heart problems)	
12. Current drug taking (e.g. THC, cocaine, smoking)	
13. Breakfast (what did the participant have for breakfast?)	
14. Significant Other Contact (name and contact number of a significant person to complete brief survey	

1. When did you go to bed last night? _____
2. How long (in minutes) did it take you to fall asleep last night? _____
3. When did you get up this morning? _____
4. How many hours of actual sleep do you get last night? _____

	Very good	Fairly good	Fairly bad	Very bad
How would you rate your overall sleep quality last night?	0	1	2	3

Interview for Ms participants

ID: _____ Date: _____

ABOUT YOUR MEDICAL HISTORY – CONTROL INTERVIEW

INSTRUCTIONS
The following set of questions is to be ASKED BY THE RESEARCHER.

6. Any prior immunotherapy? (when last used, for how long, frequency, dosage)	
7. Current medications (e.g. prednisone [i.e. corticosteroids], antidepressants, tranquilisers, antiepileptics)	
8. If steroids used in past 6 months (when, for how long, what type, dosage)	
9. Psychiatric illness (depression, anxiety disorders, schizophrenia)	
10. History of brain injury or neurological illness (e.g. TBI, MVA, alcoholism, epilepsy, stroke)	
11. Other health-related conditions (e.g. pregnancy, diabetes, heart problems)	
12. Current drug taking (e.g. THC, cocaine, smoking)	
13. Breakfast (what did the participant have for breakfast?)	
14. Significant Other Contact (name and contact number of a significant person to complete brief survey	

1. When did you go to bed last night? _____
2. How long (in minutes) did it take you to fall asleep last night? _____
3. When did you get up this morning? _____
4. How many hours of actual sleep do you get last night? _____

	Very good	Fairly good	Fairly bad	Very bad
How would you rate your overall sleep quality last night?	0	1	2	3

Appendix I

Test Battery C and D

Test Battery	Estimated Time (min)
1. Visual Analogue Scale - Fatigue	3-5
4. 10/36 Spatial Recognition Test	5-7
2. Selective Reminding Test (SRT)	8-10
3. Logical Memory I	3
5. Verbal Fluency task	4-5
9. 10/36 Spatial Recognition Test – Delayed Recall Trial	1-2
6. Paced Serial Addition Test (PASAT)	10-12
7. SRT – Delayed Recall Trial	1-2
8. Logical Memory II	1-2
10. Symbol Digits Modality Test	3
11. Connor's Continuous Performance Test – III (CPT-3)	16
12. Visual Analogue Scale - Fatigue	2-3
13. The Awareness of Social Inference Test – Short (TASIT-S)	25-30
SHORT BREAK (5-10 MINS)	
16. 10/36 Spatial Recognition Test	5-7
14. Selective Reminding Test (SRT)	8-10
15. Logical Memory I	3
17. Verbal Fluency task	4
21. 10/36 Spatial Recognition Test – Delayed Recall Trial	1-2
18. Paced Serial Addition Test (PASAT)	10-12
19. SRT – Delayed Recall Trial	1-2
20. Logical Memory II	1-2
22. Symbol Digits Modality Test	3
23. Connor's Continuous Performance Test – 3	14
24. Visual Analogue Scale - Fatigue	2-3

Note. Form A was utilised for the first half of the testing in version C and Form B first for version D. *The Awareness of Social Inference Test – Short (TASIT-S) and the second half of the test battery will be published in separate papers.

Appendix J

Raw output

Demographic Data

Group Statistics

	Type(1-ctr)	N	Mean	Std. Deviation	Std. Error Mean
AGE	CTRL	30	44.367	11.3699	2.0759
	MS	31	47.774	12.1976	2.1907
EDU	CTRL	30	12.87	1.907	.348
	MS	31	12.13	1.586	.285
FSIQ	CTRL	30	104.3833	5.26596	.96143
	MS	31	102.8687	4.96922	.89250

Group Statistics

	Type(1-ctr)	N	Mean	Std. Deviation	Std. Error Mean
Anxiety	CTRL	30	5.867	2.9447	.5376
	MS	31	7.419	4.3265	.7771
Depression	CTRL	30	3.1000	3.15518	.57605
	MS	31	6.0968	3.36011	.60349

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
AGE	Equal variances assumed	.421	.519	-1.128	59	.264	-3.4075	3.0216	-9.4537	2.6386
	Equal variances not assumed			-1.129	58.920	.263	-3.4075	3.0180	-9.4468	2.6317
EDU	Equal variances assumed	1.865	.177	1.645	59	.105	.738	.449	-.160	1.635
	Equal variances not assumed			1.640	56.395	.107	.738	.450	-.163	1.639
FSIQ	Equal variances assumed	.172	.680	1.156	59	.252	1.51462	1.31056	-1.10781	4.13705
	Equal variances not assumed			1.155	58.513	.253	1.51462	1.31183	-1.11080	4.14005

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Anxiety	Equal variances assumed	8.270	.006	-1.633	59	.108	-1.5527	.9507	-3.4550	.3497
	Equal variances not assumed			-1.643	53.026	.106	-1.5527	.9449	-3.4479	.3425
Depression	Equal variances assumed	.343	.560	-3.588	59	.001	-2.99677	.83517	-4.66794	-1.32561
	Equal variances not assumed			-3.592	58.949	.001	-2.99677	.83429	-4.66622	-1.32733

Conners Administration Times

Descriptive Statistics

	N	Range	Minimum	Maximum	Mean	Std. Deviation
CPT_3_1	61	32.00	25.00	57.00	35.4098	5.86906
CPT_3_2	61	76.00	78.00	154.00	113.9672	17.36564
Valid N (listwise)	61					

Baseline Neuropsychological Test Data

Group Statistics

	Type(1-ctr)	N	Mean	Std. Deviation	Std. Error Mean
SRemT(1)_TR	CTRL	30	52.433	8.9815	1.6398
	MS	31	46.323	12.0122	2.1575
LM(1)_IM	CTRL	30	12.867	3.7114	.6776
	MS	31	10.258	3.1619	.5679
SRecT_Toatl	CTRL	30	21.300	5.8081	1.0604
	MS	31	19.935	4.7954	.8613
Coding(1)	CTRL	30	59.167	10.7962	1.9711
	MS	31	47.387	9.9354	1.7844
PASAT_TOTAL	CTRL	30	85.167	17.0296	3.1092
	MS	31	74.097	22.5364	4.0477
SRemT(1)_TD	CTRL	30	8.700	2.5072	.4578
	MS	31	6.742	2.8632	.5142
LM(1)_DR	CTRL	30	11.933	4.0338	.7365
	MS	31	8.548	3.3351	.5990
SRecT(1)_4(Cor)	CTRL	30	7.400	2.0274	.3702
	MS	31	7.097	2.1503	.3862
WLG(1)	CTRL	30	32.533	11.1099	2.0284
	MS	31	28.710	10.3447	1.8580

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
SRemT(1)_TR	Equal variances assumed	3.836	.055	2.244	59	.029	6.1108	2.7227	.6626	11.5589
	Equal variances not assumed			2.255	55.510	.028	6.1108	2.7099	.6811	11.5404
LM(1)_IM	Equal variances assumed	.386	.537	2.958	59	.004	2.6086	.8818	.8442	4.3730
	Equal variances not assumed			2.951	56.907	.005	2.6086	.8841	.8381	4.3791
SRecT_Toatl	Equal variances assumed	1.516	.223	1.002	59	.320	1.3645	1.3618	-1.3605	4.0895
	Equal variances not assumed			.999	56.228	.322	1.3645	1.3661	-1.3719	4.1009
Coding(1)	Equal variances assumed	.502	.481	4.436	59	.000	11.7796	2.6552	6.4666	17.0926
	Equal variances not assumed			4.430	58.215	.000	11.7796	2.6589	6.4577	17.1014
PASAT_TOTAL	Equal variances assumed	.426	.517	2.159	59	.035	11.0699	5.1272	.8103	21.3295
	Equal variances not assumed			2.169	55.763	.034	11.0699	5.1040	.8445	21.2953
SRemT(1)_TD	Equal variances assumed	.462	.500	2.838	59	.006	1.9581	.6900	.5774	3.3387
	Equal variances not assumed			2.844	58.428	.006	1.9581	.6885	.5802	3.3360
LM(1)_DR	Equal variances assumed	2.343	.131	3.577	59	.001	3.3849	.9463	1.4913	5.2785
	Equal variances not assumed			3.566	56.260	.001	3.3849	.9493	1.4835	5.2864
SRecT(1)_4(Cor)	Equal variances assumed	.007	.932	.566	59	.573	.3032	.5355	-.7682	1.3747
	Equal variances not assumed			.567	58.962	.573	.3032	.5349	-.7672	1.3737
WLG(1)	Equal variances assumed	.054	.817	1.392	59	.169	3.8237	2.7474	-1.6740	9.3213
	Equal variances not assumed			1.390	58.363	.170	3.8237	2.7507	-1.6817	9.3291

Mixed Factorial ANOVA for Hit Response Time

Within-Subjects Factors

Measure: MEASURE_1

HRT	Dependent Variable
1	Con1_HRT
2	Con2_HRT

Between-Subjects Factors

		Value Label	N
Type(1-ctr)	1.0	CTRL	30
	2.0	MS	31

Descriptive Statistics

	Type(1-ctr)	Mean	Std. Deviation	N
HRT1	CTRL	52.40	10.565	30
	MS	51.10	7.427	31
	Total	51.74	9.053	61
HRT2	CTRL	48.37	8.118	30
	MS	55.06	11.975	31
	Total	51.77	10.721	61

Box's Test of Equality of Covariance Matrices[a]

Box's M	15.345
F	4.927
df1	3
df2	649994.239
Sig.	.002

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.

a. Design: Intercept + Type1ctr
Within Subjects Design: HRT

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
HRT	Pillai's Trace	.000	.001[b]	1.000	59.000	.982	.000
	Wilks' Lambda	1.000	.001[b]	1.000	59.000	.982	.000
	Hotelling's Trace	.000	.001[b]	1.000	59.000	.982	.000
	Roy's Largest Root	.000	.001[b]	1.000	59.000	.982	.000
HRT * Type1ctr	Pillai's Trace	.113	7.498[b]	1.000	59.000	.008	.113
	Wilks' Lambda	.887	7.498[b]	1.000	59.000	.008	.113
	Hotelling's Trace	.127	7.498[b]	1.000	59.000	.008	.113
	Roy's Largest Root	.127	7.498[b]	1.000	59.000	.008	.113

a. Design: Intercept + Type1ctr
Within Subjects Design: HRT

b. Exact statistic

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
HRT	1.000	.000	0	.	1.000	1.000	1.000

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + Type1ctr
Within Subjects Design: HRT

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
HRT	Sphericity Assumed	.033	1	.033	.001	.982	.000
	Greenhouse-Geisser	.033	1.000	.033	.001	.982	.000
	Huynh-Feldt	.033	1.000	.033	.001	.982	.000
	Lower-bound	.033	1.000	.033	.001	.982	.000
HRT * Type1ctr	Sphericity Assumed	488.000	1	488.000	7.498	.008	.113
	Greenhouse-Geisser	488.000	1.000	488.000	7.498	.008	.113
	Huynh-Feldt	488.000	1.000	488.000	7.498	.008	.113
	Lower-bound	488.000	1.000	488.000	7.498	.008	.113
Error(HRT)	Sphericity Assumed	3839.967	59	65.084			
	Greenhouse-Geisser	3839.967	59.000	65.084			
	Huynh-Feldt	3839.967	59.000	65.084			
	Lower-bound	3839.967	59.000	65.084			

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	HRT	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
HRT	Linear	.033	1	.033	.001	.982	.000
HRT * Type1ctr	Linear	488.000	1	488.000	7.498	.008	.113
Error(HRT)	Linear	3839.967	59	65.084			

Levene's Test of Equality of Error Variances[a]

	F	df1	df2	Sig.
HRT1	1.245	1	59	.269
HRT2	2.045	1	59	.158

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + Type1ctr
Within Subjects Design: HRT

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	326408.499	1	326408.499	2650.886	.000	.978
Type1ctr	221.843	1	221.843	1.802	.185	.030
Error	7264.780	59	123.132			

1. Type(1-ctr)

Measure: MEASURE_1

Type(1-ctr)	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
CTRL	50.383	1.433	47.517	53.250
MS	53.081	1.409	50.261	55.901

2. HRT

Measure: MEASURE_1

HRT	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
1	51.748	1.166	49.415	54.082
2	51.716	1.314	49.086	54.345

3. Type(1-ctr) * HRT

Measure: MEASURE_1

Type(1-ctr)	HRT	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
CTRL	1	52.400	1.662	49.073	55.727
	2	48.367	1.874	44.618	52.116
MS	1	51.097	1.635	47.824	54.369
	2	55.065	1.843	51.377	58.752

Group Statistics

	Type(1-ctr)	N	Mean	Std. Deviation	Std. Error Mean
HRT1	CTRL	30	52.40	10.565	1.929
	MS	31	51.10	7.427	1.334
HRT2	CTRL	30	48.37	8.118	1.482
	MS	31	55.06	11.975	2.151

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
HRT1	Equal variances assumed	1.245	.269	.559	59	.578	1.303	2.332	-3.363	5.970
	Equal variances not assumed			.556	51.895	.581	1.303	2.345	-3.403	6.010
HRT2	Equal variances assumed	2.045	.158	-2.549	59	.013	-6.698	2.628	-11.957	-1.439
	Equal variances not assumed			-2.564	52.913	.013	-6.698	2.612	-11.937	-1.459

Paired Samples Statistics

Type(1-ctr)			Mean	N	Std. Deviation	Std. Error Mean
.	Pair 1	HRT2	.	0[a]	.	.
		HRT1	.	0[a]	.	.
CTRL	Pair 1	HRT2	48.37	30	8.118	1.482
		HRT1	52.40	30	10.565	1.929
MS	Pair 1	HRT2	55.06	31	11.975	2.151
		HRT1	51.10	31	7.427	1.334

a. The correlation and t cannot be computed because there are no valid pairs.

Paired Samples Correlations[a]

Type(1-ctr)			N	Correlation	Sig.
CTRL	Pair 1	HRT2 & HRT1	30	.605	.000
MS	Pair 1	HRT2 & HRT1	31	.078	.677

a. No statistics are computed for one or more split files

Paired Samples Test[a]

Type(1-ctr)			Paired Differences					t	df	Sig. (2-tailed)
			Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
						Lower	Upper			
CTRL	Pair 1	HRT2 - HRT1	-4.033	8.588	1.568	-7.240	-.826	-2.572	29	.015
MS	Pair 1	HRT2 - HRT1	3.968	13.590	2.441	-1.017	8.953	1.626	30	.115

a. No statistics are computed for one or more split files

Mixed Factorial ANOVA for Commission Rates

Within-Subjects Factors

Measure: MEASURE_1

Comissions	Dependent Variable
1	Con1_INCom
2	Con2_INCom

Between-Subjects Factors

		Value Label	N
Type(1-ctr)	1.0	CTRL	30
	2.0	MS	31

Descriptive Statistics

	Type(1-ctr)	Mean	Std. Deviation	N
Con(1)_IN(Com)	CTRL	48.93	8.051	30
	MS	52.26	8.652	31
	Total	50.62	8.460	61
Con(2)_IN(Com)	CTRL	48.23	7.309	30
	MS	55.29	10.293	31
	Total	51.82	9.563	61

Box's Test of Equality of Covariance Matrices[a]

Box's M	5.628
F	1.807
df1	3
df2	649994.239
Sig.	.143

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.

a. Design: Intercept + Type1 ctr
Within Subjects Design: Comissions

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
Comissions	Pillai's Trace	.064	4.006[b]	1.000	59.000	.050	.064
	Wilks' Lambda	.936	4.006[b]	1.000	59.000	.050	.064
	Hotelling's Trace	.068	4.006[b]	1.000	59.000	.050	.064
	Roy's Largest Root	.068	4.006[b]	1.000	59.000	.050	.064
Comissions * Type1 ctr	Pillai's Trace	.148	10.260[b]	1.000	59.000	.002	.148
	Wilks' Lambda	.852	10.260[b]	1.000	59.000	.002	.148
	Hotelling's Trace	.174	10.260[b]	1.000	59.000	.002	.148
	Roy's Largest Root	.174	10.260[b]	1.000	59.000	.002	.148

a. Design: Intercept + Type1 ctr
Within Subjects Design: Comissions

b. Exact statistic

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
Comissions	1.000	.000	0	.	1.000	1.000	1.000

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + Type1ctr
Within Subjects Design: Comissions

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	Comissions	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Comissions	Linear	41.464	1	41.464	4.006	.050	.064
Comissions * Type1ctr	Linear	106.186	1	106.186	10.260	.002	.148
Error(Comissions)	Linear	610.634	59	10.350			

Levene's Test of Equality of Error Variances[a]

	F	df1	df2	Sig.
Con(1)_IN(Com)	.084	1	59	.772
Con(2)_IN(Com)	3.969	1	59	.051

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + Type1ctr
Within Subjects Design: Comissions

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	319464.553	1	319464.553	2286.617	.000	.975
Type1ctr	821.603	1	821.603	5.881	.018	.091
Error	8242.922	59	139.711			

1. Type(1-ctr)

Measure: MEASURE_1

Type(1-ctr)	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
CTRL	48.583	1.526	45.530	51.637
MS	53.774	1.501	50.770	56.778

2. Comissions

Measure: MEASURE_1

Comissions	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
1	50.596	1.071	48.453	52.738
2	51.762	1.146	49.468	54.056

3. Type(1-ctr) * Comissions

Measure: MEASURE_1

Type(1-ctr)	Comissions	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
CTRL	1	48.933	1.527	45.878	51.988
	2	48.233	1.634	44.963	51.504
MS	1	52.258	1.502	49.253	55.263
	2	55.290	1.608	52.073	58.507

Group Statistics

	Type(1-ctr)	N	Mean	Std. Deviation	Std. Error Mean
Con(1)_IN(Com)	CTRL	30	48.93	8.051	1.470
	MS	31	52.26	8.652	1.554
Con(2)_IN(Com)	CTRL	30	48.23	7.309	1.334
	MS	31	55.29	10.293	1.849

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Con(1)_IN(Com)	Equal variances assumed	.084	.772	-1.552	59	.126	-3.325	2.142	-7.610	.961
	Equal variances not assumed			-1.554	58.912	.125	-3.325	2.139	-7.605	.956
Con(2)_IN(Com)	Equal variances assumed	3.969	.051	-3.078	59	.003	-7.057	2.293	-11.644	-2.470
	Equal variances not assumed			-3.095	54.190	.003	-7.057	2.280	-11.628	-2.486

Paired Samples Statistics

Type(1-ctr)			Mean	N	Std. Deviation	Std. Error Mean
.	Pair 1	Con(1)_IN(Com)	.	0[a]	.	.
		Con(2)_IN(Com)	.	0[a]	.	.
CTRL	Pair 1	Con(1)_IN(Com)	48.93	30	8.051	1.470
		Con(2)_IN(Com)	48.23	30	7.309	1.334
MS	Pair 1	Con(1)_IN(Com)	52.26	31	8.652	1.554
		Con(2)_IN(Com)	55.29	31	10.293	1.849

a. The correlation and t cannot be computed because there are no valid pairs.

Paired Samples Correlations[a]

Type(1-ctr)			N	Correlation	Sig.
CTRL	Pair 1	Con(1)_IN(Com) & Con (2)_IN(Com)	30	.833	.000
MS	Pair 1	Con(1)_IN(Com) & Con (2)_IN(Com)	31	.896	.000

a. No statistics are computed for one or more split files

Paired Samples Statistics

Type(1-ctr)			Mean	N	Std. Deviation	Std. Error Mean
.	Pair 1	Con(1)_IN(Com)	.	0[a]	.	.
		Con(2)_IN(Com)	.	0[a]	.	.
CTRL	Pair 1	Con(1)_IN(Com)	48.93	30	8.051	1.470
		Con(2)_IN(Com)	48.23	30	7.309	1.334
MS	Pair 1	Con(1)_IN(Com)	52.26	31	8.652	1.554
		Con(2)_IN(Com)	55.29	31	10.293	1.849

a. The correlation and t cannot be computed because there are no valid pairs.

Paired Samples Test[a]

Type(1-ctr)			Paired Differences					t	df	Sig. (2-tailed)
			Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
						Lower	Upper			
CTRL	Pair 1	Con(1)_IN(Com) - Con(2)_IN(Com)	.700	4.489	.820	-.976	2.376	.854	29	.400
MS	Pair 1	Con(1)_IN(Com) - Con(2)_IN(Com)	-3.032	4.608	.828	-4.722	-1.342	-3.664	30	.001

a. No statistics are computed for one or more split files

Mixed Factorial ANOVA for Omissions

Within-Subjects Factors

Measure: MEASURE_1

Omissions	Dependent Variable
1	Con1_INOmi
2	Con2_INOm

Between-Subjects Factors

		Value Label	N
Type(1-ctr)	1.0	CTRL	30
	2.0	MS	31

Descriptive Statistics

	Type(1-ctr)	Mean	Std. Deviation	N
Con(1)_IN(Omi)	CTRL	47.53	8.796	30
	MS	48.32	5.558	31
	Total	47.93	7.280	61
Con(2)_IN(Om)	CTRL	47.63	8.475	30
	MS	48.81	9.130	31
	Total	48.23	8.761	61

Box's Test of Equality of Covariance Matrices[a]

Box's M	24.435
F	7.846
df1	3
df2	649994.239
Sig.	.000

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.

a. Design: Intercept + Type1 ctr
Within Subjects Design: Omissions

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
Omissions	Pillai's Trace	.002	.099[b]	1.000	59.000	.754	.002
	Wilks' Lambda	.998	.099[b]	1.000	59.000	.754	.002
	Hotelling's Trace	.002	.099[b]	1.000	59.000	.754	.002
	Roy's Largest Root	.002	.099[b]	1.000	59.000	.754	.002
Omissions * Type1ctr	Pillai's Trace	.001	.043[b]	1.000	59.000	.837	.001
	Wilks' Lambda	.999	.043[b]	1.000	59.000	.837	.001
	Hotelling's Trace	.001	.043[b]	1.000	59.000	.837	.001
	Roy's Largest Root	.001	.043[b]	1.000	59.000	.837	.001

a. Design: Intercept + Type1ctr
Within Subjects Design: Omissions

b. Exact statistic

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
Omissions	1.000	.000	0	.	1.000	1.000	1.000

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + Type1ctr
Within Subjects Design: Omissions

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Omissions	Sphericity Assumed	2.599	1	2.599	.099	.754	.002
	Greenhouse-Geisser	2.599	1.000	2.599	.099	.754	.002
	Huynh-Feldt	2.599	1.000	2.599	.099	.754	.002
	Lower-bound	2.599	1.000	2.599	.099	.754	.002
Omissions * Type1ctr	Sphericity Assumed	1.123	1	1.123	.043	.837	.001
	Greenhouse-Geisser	1.123	1.000	1.123	.043	.837	.001
	Huynh-Feldt	1.123	1.000	1.123	.043	.837	.001
	Lower-bound	1.123	1.000	1.123	.043	.837	.001
Error(Omissions)	Sphericity Assumed	1544.221	59	26.173			
	Greenhouse-Geisser	1544.221	59.000	26.173			
	Huynh-Feldt	1544.221	59.000	26.173			
	Lower-bound	1544.221	59.000	26.173			

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	Omissions	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Omissions	Linear	2.599	1	2.599	.099	.754	.002
Omissions * Type1ctr	Linear	1.123	1	1.123	.043	.837	.001
Error(Omissions)	Linear	1544.221	59	26.173			

Levene's Test of Equality of Error Variances[a]

	F	df1	df2	Sig.
Con(1)_IN(Omi)	.118	1	59	.733
Con(2)_IN(Om)	.340	1	59	.562

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + Type1ctr
Within Subjects Design: Omissions

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	281878.699	1	281878.699	2678.150	.000	.978
Type1ctr	29.355	1	29.355	.279	.599	.005
Error	6209.825	59	105.251			

1. Type(1-ctr)

Measure: MEASURE_1

Type(1-ctr)	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
CTRL	47.583	1.324	44.933	50.234
MS	48.565	1.303	45.957	51.172

2. Omissions

Measure: MEASURE_1

Omissions	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
1	47.928	.939	46.050	49.806
2	48.220	1.129	45.961	50.478

3. Type(1-ctr) * Omissions

Measure: MEASURE_1

Type(1-ctr)	Omissions	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
CTRL	1	47.533	1.338	44.855	50.211
	2	47.633	1.609	44.413	50.853
MS	1	48.323	1.317	45.688	50.957
	2	48.806	1.583	45.639	51.974

Mixed Factorial ANOVA for VAS-F

Within-Subjects Factors

Measure: MEASURE_1

VAS	Dependent Variable
1	VASF_1
2	VASF_2
3	VAS_F3

Between-Subjects Factors

		Value Label	N
Type(1-ctr)	1.0	CTRL	30
	2.0	MS	31

Descriptive Statistics

	Type(1-ctr)	Mean	Std. Deviation	N
VAS-F_1	CTRL	40.000	28.8265	30
	MS	66.419	28.5526	31
	Total	53.426	31.4104	61
VAS-F_2	CTRL	51.90	26.293	30
	MS	90.55	37.904	31
	Total	71.54	37.842	61
VAS_F(3)	CTRL	67.300	35.4568	30
	MS	114.226	35.9682	31
	Total	91.148	42.5914	61

Box's Test of Equality of Covariance Matrices[a]

Box's M	9.363
F	1.474
df1	6
df2	25143.384
Sig.	.183

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.

a. Design: Intercept + Type1 ctr
Within Subjects Design: VAS

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
VAS	Pillai's Trace	.619	47.035[b]	2.000	58.000	.000	.619
	Wilks' Lambda	.381	47.035[b]	2.000	58.000	.000	.619
	Hotelling's Trace	1.622	47.035[b]	2.000	58.000	.000	.619
	Roy's Largest Root	1.622	47.035[b]	2.000	58.000	.000	.619
VAS * Type1 ctr	Pillai's Trace	.100	3.213[b]	2.000	58.000	.047	.100
	Wilks' Lambda	.900	3.213[b]	2.000	58.000	.047	.100
	Hotelling's Trace	.111	3.213[b]	2.000	58.000	.047	.100
	Roy's Largest Root	.111	3.213[b]	2.000	58.000	.047	.100

a. Design: Intercept + Type1 ctr
Within Subjects Design: VAS

b. Exact statistic

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
VAS	.733	18.040	2	.000	.789	.821	.500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + Type1 ctr
Within Subjects Design: VAS

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
VAS	Sphericity Assumed	43024.519	2	21512.259	63.594	.000	.519
	Greenhouse-Geisser	43024.519	1.578	27262.620	63.594	.000	.519
	Huynh-Feldt	43024.519	1.642	26207.927	63.594	.000	.519
	Lower-bound	43024.519	1.000	43024.519	63.594	.000	.519
VAS * Type1 ctr	Sphericity Assumed	3245.240	2	1622.620	4.797	.010	.075
	Greenhouse-Geisser	3245.240	1.578	2056.356	4.797	.016	.075
	Huynh-Feldt	3245.240	1.642	1976.803	4.797	.015	.075
	Lower-bound	3245.240	1.000	3245.240	4.797	.032	.075
Error(VAS)	Sphericity Assumed	39916.432	118	338.275			
	Greenhouse-Geisser	39916.432	93.111	428.698			
	Huynh-Feldt	39916.432	96.858	412.113			
	Lower-bound	39916.432	59.000	676.550			

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	VAS	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
VAS	Linear	43000.906	1	43000.906	87.051	.000	.596
	Quadratic	23.613	1	23.613	.129	.720	.002
VAS * Type1 ctr	Linear	3205.562	1	3205.562	6.489	.013	.099
	Quadratic	39.678	1	39.678	.217	.643	.004
Error(VAS)	Linear	29144.569	59	493.976			
	Quadratic	10771.863	59	182.574			

Levene's Test of Equality of Error Variances[a]

	F	df1	df2	Sig.
VAS-F_1	.185	1	59	.669
VAS-F_2	3.089	1	59	.084
VAS_F(3)	.059	1	59	.809

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + Type1 ctr
Within Subjects Design: VAS

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	941376.525	1	941376.525	377.679	.000	.865
Type1 ctr	63740.853	1	63740.853	25.573	.000	.302
Error	147059.213	59	2492.529			

1. Type(1-ctr)

Measure: MEASURE_1

Type(1-ctr)	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
CTRL	53.067	5.263	42.536	63.597
MS	90.398	5.177	80.039	100.757

2. VAS

Measure: MEASURE_1

VAS	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
1	53.210	3.674	45.859	60.560
2	71.224	4.189	62.841	79.607
3	90.763	4.574	81.611	99.915

3. Type(1-ctr) * VAS

Measure: MEASURE_1

Type(1-ctr)	VAS	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
CTRL	1	40.000	5.238	29.520	50.480
	2	51.900	5.973	39.948	63.852
	3	67.300	6.521	54.251	80.349
MS	1	66.419	5.152	56.109	76.729
	2	90.548	5.876	78.791	102.306
	3	114.226	6.415	101.389	127.062

Group Statistics

	Type(1-ctr)	N	Mean	Std. Deviation	Std. Error Mean
VAS-F_1	CTRL	30	40.000	28.8265	5.2630
	MS	31	66.419	28.5526	5.1282
VAS-F_2	CTRL	30	51.90	26.293	4.800
	MS	31	90.55	37.904	6.808
VAS_F(3)	CTRL	30	67.300	35.4568	6.4735
	MS	31	114.226	35.9682	6.4601

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
VAS-F_1	Equal variances assumed	.185	.669	-3.596	59	.001	-26.4194	7.3471	-41.1209	-11.7178
	Equal variances not assumed			-3.595	58.892	.001	-26.4194	7.3483	-41.1238	-11.7149
VAS-F_2	Equal variances assumed	3.089	.084	-4.613	59	.000	-38.648	8.379	-55.414	-21.882
	Equal variances not assumed			-4.640	53.554	.000	-38.648	8.330	-55.352	-21.944
VAS_F(3)	Equal variances assumed	.059	.809	-5.130	59	.000	-46.9258	9.1476	-65.2301	-28.6215
	Equal variances not assumed			-5.131	58.979	.000	-46.9258	9.1454	-65.2259	-28.6257

Paired Samples Statistics

Type(1-ctr)			Mean	N	Std. Deviation	Std. Error Mean
.	Pair 1	VAS_F(3)	.	0[a]	.	.
		VAS-F_2	.	0[a]	.	.
	Pair 2	VAS-F_2	.	0[a]	.	.
		VAS-F_1	.	0[a]	.	.
CTRL	Pair 1	VAS_F(3)	67.300	30	35.4568	6.4735
		VAS-F_2	51.90	30	26.293	4.800
	Pair 2	VAS-F_2	51.90	30	26.293	4.800
		VAS-F_1	40.000	30	28.8265	5.2630
MS	Pair 1	VAS_F(3)	114.226	31	35.9682	6.4601
		VAS-F_2	90.55	31	37.904	6.808
	Pair 2	VAS-F_2	90.55	31	37.904	6.808
		VAS-F_1	66.419	31	28.5526	5.1282

a. The correlation and t cannot be computed because there are no valid pairs.

Paired Samples Correlations[a]

Type(1-ctr)			N	Correlation	Sig.
CTRL	Pair 1	VAS_F(3) & VAS-F_2	30	.797	.000
	Pair 2	VAS-F_2 & VAS-F_1	30	.649	.000
MS	Pair 1	VAS_F(3) & VAS-F_2	31	.889	.000
	Pair 2	VAS-F_2 & VAS-F_1	31	.682	.000

a. No statistics are computed for one or more split files

Paired Samples Test[a]

Type(1-ctr)			Paired Differences					t	df	Sig. (2-tailed)
			Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
						Lower	Upper			
CTRL	Pair 1	VAS_F(3) - VAS-F_2	15.4000	21.5096	3.9271	7.3682	23.4318	3.921	29	.000
	Pair 2	VAS-F_2 - VAS-F_1	11.9000	23.1983	4.2354	3.2376	20.5624	2.810	29	.009
MS	Pair 1	VAS_F(3) - VAS-F_2	23.6774	17.4860	3.1406	17.2635	30.0913	7.539	30	.000
	Pair 2	VAS-F_2 - VAS-F_1	24.1290	27.8469	5.0014	13.9147	34.3434	4.824	30	.000

a. No statistics are computed for one or more split files

MFIS *t*-test

Group Statistics

	Type(1-ctr)	N	Mean	Std. Deviation	Std. Error Mean
MFIS	CTRL	30	9.67	5.088	.929
	MS	31	15.58	7.316	1.314

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
MFIS	Equal variances assumed	3.283	.075	-3.654	59	.001	-5.914	1.618	-9.153	-2.675
	Equal variances not assumed			-3.675	53.624	.001	-5.914	1.609	-9.141	-2.687

Regression Analysis

Model Summary[a,c]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics					Durbin-Watson
					R Square Change	F Change	df1	df2	Sig. F Change	
1	.215[b]	.046	-.022	7.508	.046	.677	2	28	.516	2.256

a. Type(1-ctr) = MS

b. Predictors: (Constant), MFIS, VAS-F_2

c. Dependent Variable: HRT1

ANOVA[a,b]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	76.339	2	38.170	.677	.516[c]
	Residual	1578.371	28	56.370		
	Total	1654.710	30			

a. Type(1-ctr) = MS

b. Dependent Variable: HRT1

c. Predictors: (Constant), MFIS, VAS-F_2

Coefficients[a,b]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Correlations			Collinearity Statistics	
		B	Std. Error	Beta			Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	50.955	4.040		12.613	.000					
	VAS-F_2	-.033	.038	-.170	-.868	.393	-.104	-.162	-.160	.890	1.123
	MFIS	.202	.199	.199	1.019	.317	.143	.189	.188	.890	1.123

a. Type(1-ctr) = MS

b. Dependent Variable: HRT1

Model Summary[a,c]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics					Durbin-Watson
					R Square Change	F Change	df1	df2	Sig. F Change	
1	.320[b]	.102	.038	8.486	.102	1.593	2	28	.221	2.197

a. Type(1-ctr) = MS

b. Predictors: (Constant), MFIS, VAS-F_2

c. Dependent Variable: Con(1)_IN(Com)

ANOVA[a,b]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	229.430	2	114.715	1.593	.221[c]
	Residual	2016.506	28	72.018		
	Total	2245.935	30			

a. Type(1-ctr) = MS

b. Dependent Variable: Con(1)_IN(Com)

c. Predictors: (Constant), MFIS, VAS-F_2

Coefficients[a,b]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Correlations			Collinearity Statistics	
		B	Std. Error	Beta			Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	44.585	4.566		9.764	.000					
	VAS-F_2	.047	.043	.204	1.076	.291	.266	.199	.193	.890	1.123
	MFIS	.222	.224	.187	.987	.332	.255	.183	.177	.890	1.123

a. Type(1-ctr) = MS

b. Dependent Variable: Con(1)_IN(Com)

Model Summary[a,c]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics					Durbin-Watson
					R Square Change	F Change	df1	df2	Sig. F Change	
1	.251[b]	.063	-.004	11.999	.063	.939	2	28	.403	1.757

a. Type(1-ctr) = MS

b. Predictors: (Constant), MFIS, VAS_F(3)

c. Dependent Variable: HRT2

ANOVA[a,b]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	270.452	2	135.226	.939	.403[c]
	Residual	4031.419	28	143.979		
	Total	4301.871	30			

a. Type(1-ctr) = MS

b. Dependent Variable: HRT2

c. Predictors: (Constant), MFIS, VAS_F(3)

Coefficients[a,b]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Correlations			Collinearity Statistics	
		B	Std. Error	Beta			Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	58.714	7.893		7.439	.000					
	VAS_F(3)	-.073	.063	-.220	-1.168	.253	-.175	-.216	-.214	.939	1.065
	MFIS	.304	.309	.186	.983	.334	.131	.183	.180	.939	1.065

a. Type(1-ctr) = MS

b. Dependent Variable: HRT2

Model Summary[a,c]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics					Durbin-Watson
					R Square Change	F Change	df1	df2	Sig. F Change	
1	.477[b]	.227	.172	9.365	.227	4.121	2	28	.027	2.030

a. Type(1-ctr) = MS

b. Predictors: (Constant), MFIS, VAS_F(3)

c. Dependent Variable: Con(2)_IN(Com)

ANOVA[a,b]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	722.814	2	361.407	4.121	.027[c]
	Residual	2455.573	28	87.699		
	Total	3178.387	30			

a. Type(1-ctr) = MS

b. Dependent Variable: Con(2)_IN(Com)

c. Predictors: (Constant), MFIS, VAS_F(3)

Coefficients[a,b]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	Correlations			Collinearity Statistics	
		B	Std. Error	Beta			Zero-order	Partial	Part	Tolerance	VIF
1	(Constant)	38.280	6.160		6.214	.000					
	VAS_F(3)	.113	.049	.394	2.296	.029	.440	.398	.381	.939	1.065
	MFIS	.266	.241	.189	1.103	.279	.286	.204	.183	.939	1.065

a. Type(1-ctr) = MS

b. Dependent Variable: Con(2)_IN(Com)

Insight Data

Group Statistics

	Type(1-ctr)	N	Mean	Std. Deviation	Std. Error Mean
COM1_Inshight_VAS2	CTRL	30	.3193	1.22504	.22366
	MS	31	-.3090	1.22628	.22025
HRT1_Inshight_VAS2	CTRL	30	.5922	1.20620	.22022
	MS	31	-.5731	1.35890	.24406
COM_INSIGHT_VAS3	CTRL	30	.1849	1.08725	.19850
	MS	31	-.1789	1.03503	.18590
HRT_INSIGHT_VAS3	CTRL	30	.2424	.88157	.16095
	MS	31	-.2346	1.51331	.27180
COM_INSIGHT_MFIS	CTRL	30	.0581	.91921	.16782
	MS	31	-.0562	1.27283	.22861
HRT_INSIGHT_MFIS	CTRL	30	.1156	.89991	.16430
	MS	31	-.1119	1.43172	.25714

Mann- Whitney Test

Ranks

	Type(1-ctr)	N	Mean Rank	Sum of Ranks
HRT_INSIGHT_VAS3	CTRL	30	35.40	1062.00
	MS	31	26.74	829.00
	Total	61		

Test Statistics[a]

	HRT_INSIGHT_VAS3
Mann-Whitney U	333.000
Wilcoxon W	829.000
Z	-1.904
Asymp. Sig. (2-tailed)	.057

a. Grouping Variable: Type(1-ctr)

Appendix K

Analysis Conducted with transformed data

Mixed Factorial ANOVA for Hit Response Data

Within-Subjects Factors

Measure: MEASURE_1

SQRT_HRT	Dependent Variable
1	XHR1_SQRT
2	XHR2_SQRT

Between-Subjects Factors

		Value Label	N
Type(1-ctr)	1.0	CTRL	30
	2.0	MS	31

Descriptive Statistics

	Type(1-ctr)	Mean	Std. Deviation	N
XHR1_SQRT	CTRL	7.2001	.76021	30
	MS	7.1305	.51168	31
	Total	7.1647	.64146	61
XHR2_SQRT	CTRL	6.9295	.60093	30
	MS	7.3829	.75868	31
	Total	7.1599	.71734	61

Box's Test of Equality of Covariance Matrices[a]

Box's M	12.943
F	4.156
df1	3
df2	649994.239
Sig.	.006

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.

a. Design: Intercept + Type1ctr
Within Subjects Design: SQRT_HRT

Levene's Test of Equality of Error Variances[a]

	F	df1	df2	Sig.
XHR1_SQRT	1.178	1	59	.282
XHR2_SQRT	1.124	1	59	.293

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + Type1 ctr
Within Subjects Design: SQRT_HRT

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	6254.006	1	6254.006	10350.047	.000	.994
Type1 ctr	1.123	1	1.123	1.858	.178	.031
Error	35.651	59	.604			

1. Type(1-ctr)

Measure: MEASURE_1

Type(1-ctr)	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
CTRL	7.065	.100	6.864	7.266
MS	7.257	.099	7.059	7.454

2. SQRT_HRT

Measure: MEASURE_1

SQRT_HRT	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
1	7.165	.083	7.000	7.331
2	7.156	.088	6.980	7.332

3. Type(1-ctr) * SQRT_HRT

Measure: MEASURE_1

Type(1-ctr)	SQRT_HRT	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
CTRL	1	7.200	.118	6.964	7.436
	2	6.929	.125	6.679	7.180
MS	1	7.130	.116	6.898	7.363
	2	7.383	.123	7.136	7.629

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
SQRT_HRT	Pillai's Trace	.000	.009[b]	1.000	59.000	.925	.000
	Wilks' Lambda	1.000	.009[b]	1.000	59.000	.925	.000
	Hotelling's Trace	.000	.009[b]	1.000	59.000	.925	.000
	Roy's Largest Root	.000	.009[b]	1.000	59.000	.925	.000
SQRT_HRT * Type1ctr	Pillai's Trace	.111	7.367[b]	1.000	59.000	.009	.111
	Wilks' Lambda	.889	7.367[b]	1.000	59.000	.009	.111
	Hotelling's Trace	.125	7.367[b]	1.000	59.000	.009	.111
	Roy's Largest Root	.125	7.367[b]	1.000	59.000	.009	.111

a. Design: Intercept + Type1ctr
Within Subjects Design: SQRT_HRT

b. Exact statistic

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
SQRT_HRT	1.000	.000	0	.	1.000	1.000	1.000

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + Type1ctr
Within Subjects Design: SQRT_HRT

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
SQRT_HRT	Sphericity Assumed	.003	1	.003	.009	.925	.000
	Greenhouse-Geisser	.003	1.000	.003	.009	.925	.000
	Huynh-Feldt	.003	1.000	.003	.009	.925	.000
	Lower-bound	.003	1.000	.003	.009	.925	.000
SQRT_HRT * Type1ctr	Sphericity Assumed	2.086	1	2.086	7.367	.009	.111
	Greenhouse-Geisser	2.086	1.000	2.086	7.367	.009	.111
	Huynh-Feldt	2.086	1.000	2.086	7.367	.009	.111
	Lower-bound	2.086	1.000	2.086	7.367	.009	.111
Error(SQRT_HRT)	Sphericity Assumed	16.704	59	.283			
	Greenhouse-Geisser	16.704	59.000	.283			
	Huynh-Feldt	16.704	59.000	.283			
	Lower-bound	16.704	59.000	.283			

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	SQRT_HRT	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
SQRT_HRT	Linear	.003	1	.003	.009	.925	.000
SQRT_HRT * Type1ctr	Linear	2.086	1	2.086	7.367	.009	.111
Error(SQRT_HRT)	Linear	16.704	59	.283			

Mixed Factorial ANOVA for Omissions Data

3. Type(1-ctr) * SQRT_HRT

Measure: MEASURE_1

Type(1-ctr)	SQRT_HRT	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
CTRL	1	7.200	.118	6.964	7.436
	2	6.929	.125	6.679	7.180
MS	1	7.130	.116	6.898	7.363
	2	7.383	.123	7.136	7.629

Within-Subjects Factors

Measure: MEASURE_1

SQRT_OMS	Dependent Variable
1	X_om_1SQ
2	X_om_2SQ

Between-Subjects Factors

		Value Label	N
Type(1-ctr)	1.0	CTRL	30
	2.0	MS	31

Descriptive Statistics

	Type(1-ctr)	Mean	Std. Deviation	N
X_om_1SQ	CTRL	6.8729	.55342	30
	MS	6.9415	.37825	31
	Total	6.9078	.46985	61
X_om_2SQ	CTRL	6.8819	.53115	30
	MS	6.9629	.57890	31
	Total	6.9231	.55280	61

Box's Test of Equality of Covariance Matrices[a]

Box's M	19.268
F	6.187
df1	3
df2	649994.239
Sig.	.000

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.

a. Design: Intercept + Type1ctr
Within Subjects Design: SQRT_OMS

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
SQRT_OMS	Pillai's Trace	.001	.064[b]	1.000	59.000	.801	.001
	Wilks' Lambda	.999	.064[b]	1.000	59.000	.801	.001
	Hotelling's Trace	.001	.064[b]	1.000	59.000	.801	.001
	Roy's Largest Root	.001	.064[b]	1.000	59.000	.801	.001
SQRT_OMS * Type1ctr	Pillai's Trace	.000	.011[b]	1.000	59.000	.918	.000
	Wilks' Lambda	1.000	.011[b]	1.000	59.000	.918	.000
	Hotelling's Trace	.000	.011[b]	1.000	59.000	.918	.000
	Roy's Largest Root	.000	.011[b]	1.000	59.000	.918	.000

a. Design: Intercept + Type1ctr
Within Subjects Design: SQRT_OMS

b. Exact statistic

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
SQRT_OMS	1.000	.000	0	.	1.000	1.000	1.000

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + Type1ctr
Within Subjects Design: SQRT_OMS

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
SQRT_OMS	Sphericity Assumed	.007	1	.007	.064	.801	.001
	Greenhouse-Geisser	.007	1.000	.007	.064	.801	.001
	Huynh-Feldt	.007	1.000	.007	.064	.801	.001
	Lower-bound	.007	1.000	.007	.064	.801	.001
SQRT_OMS * Type1ctr	Sphericity Assumed	.001	1	.001	.011	.918	.000
	Greenhouse-Geisser	.001	1.000	.001	.011	.918	.000
	Huynh-Feldt	.001	1.000	.001	.011	.918	.000
	Lower-bound	.001	1.000	.001	.011	.918	.000
Error(SQRT_OMS)	Sphericity Assumed	6.477	59	.110			
	Greenhouse-Geisser	6.477	59.000	.110			
	Huynh-Feldt	6.477	59.000	.110			
	Lower-bound	6.477	59.000	.110			

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	SQRT_OMS	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
SQRT_OMS	Linear	.007	1	.007	.064	.801	.001
SQRT_OMS * Type1ctr	Linear	.001	1	.001	.011	.918	.000
Error(SQRT_OMS)	Linear	6.477	59	.110			

Levene's Test of Equality of Error Variances[a]

	F	df1	df2	Sig.
X_om_1SQ	.039	1	59	.844
X_om_2SQ	.354	1	59	.554

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + Type1ctr
Within Subjects Design: SQRT_OMS

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	5831.810	1	5831.810	13800.389	.000	.996
Type1ctr	.170	1	.170	.403	.528	.007
Error	24.932	59	.423			

1. Type(1-ctr)

Measure: MEASURE_1

Type(1-ctr)	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
CTRL	6.877	.084	6.709	7.045
MS	6.952	.083	6.787	7.117

2. SQRT_OMS

Measure: MEASURE_1

SQRT_OMS	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
1	6.907	.061	6.786	7.028
2	6.922	.071	6.780	7.065

3. Type(1-ctr) * SQRT_OMS

Measure: MEASURE_1

Type(1-ctr)	SQRT_OMS	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
CTRL	1	6.873	.086	6.700	7.046
	2	6.882	.102	6.679	7.085
MS	1	6.941	.085	6.772	7.111
	2	6.963	.100	6.763	7.163

Comparison of Verbal Fluency

3. Type(1-ctr) * SQRT_OMS

Measure: MEASURE_1

Type(1-ctr)	SQRT_OMS	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
CTRL	1	6.873	.086	6.700	7.046
	2	6.882	.102	6.679	7.085
MS	1	6.941	.085	6.772	7.111
	2	6.963	.100	6.763	7.163

Group Statistics

	Type(1-ctr)	N	Mean	Std. Deviation	Std. Error Mean
WLG(1)	CTRL	30	32.533	11.1099	2.0284
	MS	31	28.710	10.3447	1.8580
X_VF_SQRT	CTRL	30	5.6399	.86597	.15810
	MS	31	5.2811	.92034	.16530

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
WLG(1)	Equal variances assumed	.054	.817	1.392	59	.169	3.8237	2.7474	-1.6740	9.3213
	Equal variances not assumed			1.390	58.363	.170	3.8237	2.7507	-1.6817	9.3291
X_VF_SQRT	Equal variances assumed	.380	.540	1.567	59	.122	.35880	.22897	-.09937	.81697
	Equal variances not assumed			1.569	58.955	.122	.35880	.22874	-.09891	.81651

Appendix L

Raw data stratified by Impairment

Group Statistics

	Impaired	N	Mean	Std. Deviation	Std. Error Mean
AGE	not impaired	13	42.846	11.0291	3.0589
	Impaired	17	52.471	11.3585	2.7548
EDU	not impaired	13	12.23	1.641	.455
	Impaired	17	12.00	1.620	.393
FSIQ	not impaired	13	102.8531	4.31426	1.19656
	Impaired	17	102.9200	5.68411	1.37860
Anxiety	not impaired	13	6.769	3.8763	1.0751
	Impaired	17	7.706	4.7535	1.1529
Depression	not impaired	13	5.4615	3.43063	.95149
	Impaired	17	6.5294	3.42997	.83189

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
AGE	Equal variances assumed	.019	.891	-2.329	28	.027	-9.6244	4.1333	-18.0912	-1.1577
	Equal variances not assumed			-2.338	26.356	.027	-9.6244	4.1166	-18.0806	-1.1683
EDU	Equal variances assumed	.263	.612	.384	28	.704	.231	.600	-.999	1.460
	Equal variances not assumed			.384	25.806	.704	.231	.601	-1.006	1.467
FSIQ	Equal variances assumed	1.793	.191	-.035	28	.972	-.06692	1.89448	-3.94758	3.81374
	Equal variances not assumed			-.037	28.000	.971	-.06692	1.82546	-3.80620	3.67236
Anxiety	Equal variances assumed	2.249	.145	-.578	28	.568	-.9367	1.6208	-4.2566	2.3833
	Equal variances not assumed			-.594	27.848	.557	-.9367	1.5764	-4.1665	2.2932
Depression	Equal variances assumed	.118	.734	-.845	28	.405	-1.06787	1.26384	-3.65672	1.52098
	Equal variances not assumed			-.845	25.975	.406	-1.06787	1.26387	-3.66592	1.53017

Mixed Factorial ANOVA for Hit Response Time

Within-Subjects Factors

Measure: MEASURE_1

HRT	Dependent Variable
1	Con1_HRT
2	Con2_HRT

Between-Subjects Factors

		Value Label	N
Impaired	1.00	not impaired	13
	2.00	Impaired	17

Descriptive Statistics

	Impaired	Mean	Std. Deviation	N
HRT1	not impaired	49.92	7.147	13
	Impaired	52.53	7.526	17
	Total	51.40	7.356	30
HRT2	not impaired	54.23	12.807	13
	Impaired	56.29	11.719	17
	Total	55.40	12.030	30

Box's Test of Equality of Covariance Matrices[a]

Box's M	1.903
F	.584
df1	3
df2	85663.475
Sig.	.626

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.

a. Design: Intercept + Impaired
Within Subjects Design: HRT

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
HRT	Pillai's Trace	.080	2.427[b]	1.000	28.000	.130	.080
	Wilks' Lambda	.920	2.427[b]	1.000	28.000	.130	.080
	Hotelling's Trace	.087	2.427[b]	1.000	28.000	.130	.080
	Roy's Largest Root	.087	2.427[b]	1.000	28.000	.130	.080
HRT * Impaired	Pillai's Trace	.000	.011[b]	1.000	28.000	.917	.000
	Wilks' Lambda	1.000	.011[b]	1.000	28.000	.917	.000
	Hotelling's Trace	.000	.011[b]	1.000	28.000	.917	.000
	Roy's Largest Root	.000	.011[b]	1.000	28.000	.917	.000

a. Design: Intercept + Impaired
Within Subjects Design: HRT

b. Exact statistic

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
HRT	1.000	.000	0	.	1.000	1.000	1.000

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + Impaired
Within Subjects Design: HRT

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
HRT	Sphericity Assumed	240.019	1	240.019	2.427	.130	.080
	Greenhouse-Geisser	240.019	1.000	240.019	2.427	.130	.080
	Huynh-Feldt	240.019	1.000	240.019	2.427	.130	.080
	Lower-bound	240.019	1.000	240.019	2.427	.130	.080
HRT * Impaired	Sphericity Assumed	1.086	1	1.086	.011	.917	.000
	Greenhouse-Geisser	1.086	1.000	1.086	.011	.917	.000
	Huynh-Feldt	1.086	1.000	1.086	.011	.917	.000
	Lower-bound	1.086	1.000	1.086	.011	.917	.000
Error(HRT)	Sphericity Assumed	2768.914	28	98.890			
	Greenhouse-Geisser	2768.914	28.000	98.890			
	Huynh-Feldt	2768.914	28.000	98.890			
	Lower-bound	2768.914	28.000	98.890			

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	HRT	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
HRT	Linear	240.019	1	240.019	2.427	.130	.080
HRT * Impaired	Linear	1.086	1	1.086	.011	.917	.000
Error(HRT)	Linear	2768.914	28	98.890			

Levene's Test of Equality of Error Variances[a]

	F	df1	df2	Sig.
HRT1	.034	1	28	.856
HRT2	.005	1	28	.946

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + Impaired
Within Subjects Design: HRT

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	167073.652	1	167073.652	1604.229	.000	.983
Impaired	80.319	1	80.319	.771	.387	.027
Error	2916.081	28	104.146			

1. HRT

Measure: MEASURE_1

HRT	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
1	51.226	1.357	48.447	54.006
2	55.262	2.247	50.660	59.865

2. Impaired

Measure: MEASURE_1

Impaired	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
not impaired	52.077	2.001	47.977	56.177
Impaired	54.412	1.750	50.827	57.997

3. Impaired * HRT

Measure: MEASURE_1

Impaired	HRT	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
not impaired	1	49.923	2.043	45.738	54.108
	2	54.231	3.383	47.301	61.161
Impaired	1	52.529	1.786	48.870	56.189
	2	56.294	2.958	50.234	62.354

Mixed Factorial ANOVA for Hit Response Time

Within-Subjects Factors

Measure: MEASURE_1

Coms	Dependent Variable
1	Con1_INCom
2	Con2_INCom

Between-Subjects Factors

		Value Label	N
Impaired	1.00	not impaired	13
	2.00	Impaired	17

Descriptive Statistics

	Impaired	Mean	Std. Deviation	N
Con(1)_IN(Com)	not impaired	53.77	9.628	13
	Impaired	51.47	8.117	17
	Total	52.47	8.721	30
Con(2)_IN(Com)	not impaired	55.54	11.259	13
	Impaired	55.06	10.170	17
	Total	55.27	10.468	30

Box's Test of Equality of Covariance Matrices[a]

Box's M	1.364
F	.419
df1	3
df2	85663.475
Sig.	.740

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.

a. Design: Intercept + Impaired
Within Subjects Design: Coms

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
Coms	Pillai's Trace	.273	10.526[b]	1.000	28.000	.003	.273
	Wilks' Lambda	.727	10.526[b]	1.000	28.000	.003	.273
	Hotelling's Trace	.376	10.526[b]	1.000	28.000	.003	.273
	Roy's Largest Root	.376	10.526[b]	1.000	28.000	.003	.273
Coms * Impaired	Pillai's Trace	.042	1.213[b]	1.000	28.000	.280	.042
	Wilks' Lambda	.958	1.213[b]	1.000	28.000	.280	.042
	Hotelling's Trace	.043	1.213[b]	1.000	28.000	.280	.042
	Roy's Largest Root	.043	1.213[b]	1.000	28.000	.280	.042

a. Design: Intercept + Impaired
Within Subjects Design: Coms

b. Exact statistic

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
Coms	1.000	.000	0	.	1.000	1.000	1.000

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + Impaired
Within Subjects Design: Coms

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Coms	Sphericity Assumed	105.721	1	105.721	10.526	.003	.273
	Greenhouse-Geisser	105.721	1.000	105.721	10.526	.003	.273
	Huynh-Feldt	105.721	1.000	105.721	10.526	.003	.273
	Lower-bound	105.721	1.000	105.721	10.526	.003	.273
Coms * Impaired	Sphericity Assumed	12.187	1	12.187	1.213	.280	.042
	Greenhouse-Geisser	12.187	1.000	12.187	1.213	.280	.042
	Huynh-Feldt	12.187	1.000	12.187	1.213	.280	.042
	Lower-bound	12.187	1.000	12.187	1.213	.280	.042
Error(Coms)	Sphericity Assumed	281.213	28	10.043			
	Greenhouse-Geisser	281.213	28.000	10.043			
	Huynh-Feldt	281.213	28.000	10.043			
	Lower-bound	281.213	28.000	10.043			

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	Coms	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Coms	Linear	105.721	1	105.721	10.526	.003	.273
Coms * Impaired	Linear	12.187	1	12.187	1.213	.280	.042
Error(Coms)	Linear	281.213	28	10.043			

Levene's Test of Equality of Error Variances[a]

	F	df1	df2	Sig.
Con(1)_IN(Com)	.601	1	28	.445
Con(2)_IN(Com)	.595	1	28	.447

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + Impaired
Within Subjects Design: Coms

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	171590.498	1	171590.498	949.231	.000	.971
Impaired	28.431	1	28.431	.157	.695	.006
Error	5061.502	28	180.768			

1. Impaired

Measure: MEASURE_1

Impaired	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
not impaired	54.654	2.637	49.253	60.055
Impaired	53.265	2.306	48.541	57.988

2. Coms

Measure: MEASURE_1

Coms	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
1	52.620	1.620	49.301	55.939
2	55.299	1.962	51.280	59.318

3. Impaired * Coms

Measure: MEASURE_1

Impaired	Coms	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
not impaired	1	53.769	2.440	48.772	58.767
	2	55.538	2.954	49.488	61.589
Impaired	1	51.471	2.133	47.100	55.841
	2	55.059	2.583	49.767	60.350

Mixed Factorial ANOVA for Hit Response Time

Within-Subjects Factors

Measure: MEASURE_1

Oms	Dependent Variable
1	Con1_INOmi
2	Con2_INOm

Between-Subjects Factors

		Value Label	N
Impaired	1.00	not impaired	13
	2.00	Impaired	17

Descriptive Statistics

	Impaired	Mean	Std. Deviation	N
Con(1)_IN(Omi)	not impaired	47.00	3.367	13
	Impaired	49.35	6.846	17
	Total	48.33	5.653	30
Con(2)_IN(Om)	not impaired	46.08	2.985	13
	Impaired	51.12	11.704	17
	Total	48.93	9.258	30

Box's Test of Equality of Covariance Matrices[a]

Box's M	26.575
F	8.154
df1	3
df2	85663.475
Sig.	.000

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.

a. Design: Intercept + Impaired
Within Subjects Design: Oms

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
Oms	Pillai's Trace	.002	.058[b]	1.000	28.000	.811	.002
	Wilks' Lambda	.998	.058[b]	1.000	28.000	.811	.002
	Hotelling's Trace	.002	.058[b]	1.000	28.000	.811	.002
	Roy's Largest Root	.002	.058[b]	1.000	28.000	.811	.002
Oms * Impaired	Pillai's Trace	.021	.595[b]	1.000	28.000	.447	.021
	Wilks' Lambda	.979	.595[b]	1.000	28.000	.447	.021
	Hotelling's Trace	.021	.595[b]	1.000	28.000	.447	.021
	Roy's Largest Root	.021	.595[b]	1.000	28.000	.447	.021

a. Design: Intercept + Impaired
Within Subjects Design: Oms

b. Exact statistic

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
Oms	1.000	.000	0	.	1.000	1.000	1.000

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + Impaired
Within Subjects Design: Oms

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Oms	Sphericity Assumed	2.609	1	2.609	.058	.811	.002
	Greenhouse-Geisser	2.609	1.000	2.609	.058	.811	.002
	Huynh-Feldt	2.609	1.000	2.609	.058	.811	.002
	Lower-bound	2.609	1.000	2.609	.058	.811	.002
Oms * Impaired	Sphericity Assumed	26.609	1	26.609	.595	.447	.021
	Greenhouse-Geisser	26.609	1.000	26.609	.595	.447	.021
	Huynh-Feldt	26.609	1.000	26.609	.595	.447	.021
	Lower-bound	26.609	1.000	26.609	.595	.447	.021
Error(Oms)	Sphericity Assumed	1252.991	28	44.750			
	Greenhouse-Geisser	1252.991	28.000	44.750			
	Huynh-Feldt	1252.991	28.000	44.750			
	Lower-bound	1252.991	28.000	44.750			

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	Oms	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Oms	Linear	2.609	1	2.609	.058	.811	.002
Oms * Impaired	Linear	26.609	1	26.609	.595	.447	.021
Error(Oms)	Linear	1252.991	28	44.750			

Levene's Test of Equality of Error Variances[a]

	F	df1	df2	Sig.
Con(1)_IN(Omi)	2.894	1	28	.100
Con(2)_IN(Om)	4.479	1	28	.043

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + Impaired
Within Subjects Design: Oms

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	137980.021	1	137980.021	2000.146	.000	.986
Impaired	201.354	1	201.354	2.919	.099	.094
Error	1931.579	28	68.985			

1. Impaired

Measure: MEASURE_1

Impaired	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
not impaired	46.538	1.629	43.202	49.875
Impaired	50.235	1.424	47.318	53.153

2. Oms

Measure: MEASURE_1

Oms	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
1	48.176	1.036	46.054	50.299
2	48.597	1.669	45.178	52.016

3. Impaired * Oms

Measure: MEASURE_1

Impaired	Oms	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
not impaired	1	47.000	1.560	43.804	50.196
	2	46.077	2.513	40.929	51.225
Impaired	1	49.353	1.364	46.558	52.147
	2	51.118	2.198	46.616	55.619

Insight Analysis

Group Statistics

	Impaired	N	Mean	Std. Deviation	Std. Error Mean
COM1_Inshight_VAS2	not impaired	13	.0589	1.22881	.34081
	Impaired	17	-.5213	1.20125	.29135
HRT1_Inshight_VAS2	not impaired	13	-.5134	1.50634	.41778
	Impaired	17	-.5340	1.27536	.30932
COM_INSIGHT_VAS3	not impaired	13	.0636	.91945	.25501
	Impaired	17	-.3677	1.13524	.27534
HRT_INSIGHT_VAS3	not impaired	13	-.0958	1.74156	.48302
	Impaired	17	-.2845	1.39414	.33813
COM_INSIGHT_MFIS	not impaired	13	-.0131	1.68979	.46866
	Impaired	17	-.0815	.94493	.22918
HRT_INSIGHT_MFIS	not impaired	13	-.1725	1.68461	.46723
	Impaired	17	.0017	1.27146	.30837